Booklet outlines

Welcome to the Laboratory for Integrated Micro-Mechatronic Systems (LIMMS/CNRS-IIS IRL 2820)

Creation and achievements

LIMMS (Laboratory for Integrated Micro Mechatronic Systems) is a joint laboratory between CNRS Engineering Institute and the University of Tokyo (IIS - Institute of Industrial Science). LIMMS researchers are hosted in 17 research groups mainly located on Komaba Research Campus of the University of Tokyo. Since its creation in 1995 the laboratory has been working in the field of micro/nanotechnologies and BioMEMS.

LIMMS was created in 1995 as a cooperation unit between CNRS (then SPI Department and now CNRS Engineering). Soon after it was established, the laboratory benefited largely from the strong support from the Japan Society for the Promotion of Science (JSPS).

In 2000, LIMMS was relocated, together with IIS, to the Komaba Research Campus (Tokyo/MeguroKu), where exceptional technological facilities are provided.

1995
creation of LIMMS

3
research axis

Energy
Quantum & Molecular Tech.
Bio-engineering

4
main grants

2019-2024 JSPS C2C
2019-2025 CREST-JST
2022-2029 PEPR MoleculArchiv
2024-2030 PEPR MED-OOC

2025 - 2026
44
papers

15
conferences

4
EPI

Since 2015
392
papers

317
conferences

2025 - 2026
21
contracts

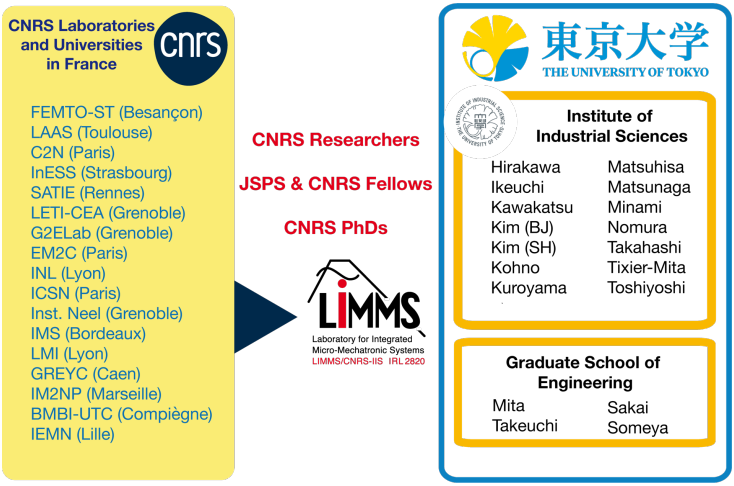
102
people
involved in LIMMS activities

Since 1995
470
people welcome

52 CNRS researchers
31 CNRS post-doc
82 JSPS post-doc
14 IIS post doc
10 CNRS Research Eng.
35 PhD students
108 Internships
22 administrative staff
...

2023
ecoLIMMS started

16
New research teams created in France by former LIMMS members



Since the IRL 2820 foundation in 2004 (IRL= International Research Laboratory), LIMMS has been eligible to apply for French, Japanese and European research projects and grants-in-aid.

After successful review meetings, LIMMS was renewed for three terms (2010-2030). During this period, LIMMS extended its structure to European partners through EUJO-LIMMS, a project funded by the European Union (Dec. 2011 - May.2016) along with a first Core-to-Core program (April 2012 - March 2017) of the JSPS.

In 2014, LIMMS took a new step in its development by inaugurating a mirror location in Lille (France) inside a hospital. The SMMiL-E project, Seeding Microsystems in Medicine in Lille, first research location of IIS out of Japan, gathers IIS, CNRS, Centre Oscar Lambret and Lille University.

In 2017, LIMMS was involved as a partner of the iLite consortium (for innovation in Liver tissue engineering, 2017-2022), an university research hospital project, granted by the French program-investment for the future (Program Investissement d'Avenir).

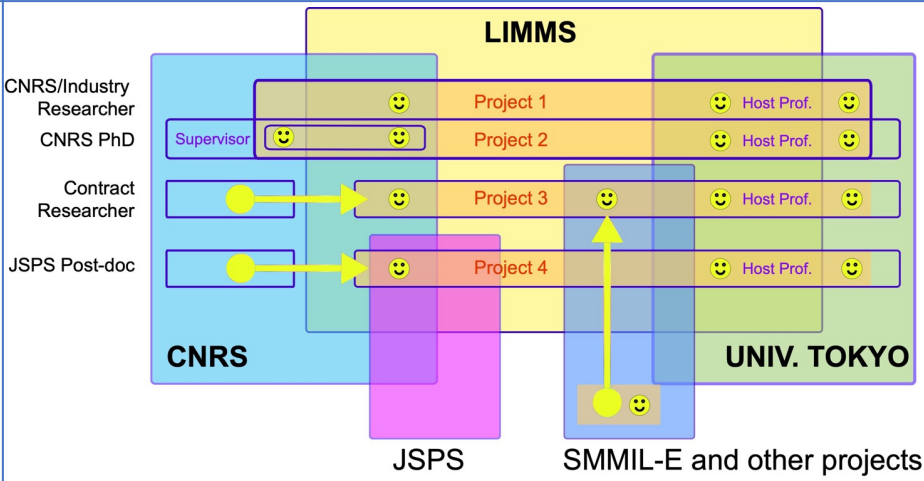
In 2019, a second JSPS Core-to-Core program (JSPS) was assigned to LIMMS (April 2019-March 2024) to promote the interactions more specifically in Bio-oriented activities with SMMiL-E and the partners of iLite.

In 2020, a CREST (JST) project targeting thermal management in silicon devices was attributed to LIMMS (October 2019-March 2025).

In 2021, an Integrate Research Network 'LIMMS Kiko' (period 2021-2031) of the University of Tokyo centered on LIMMS activities was started to extend connections with 55 Japanese professors from 8 Institutes and Schools including fields such as engineering, medicine, information science and philosophy.

In 2022, LIMMS was involved in the MoleculArxiv PEPR (Programme et Equipements Prioritaires de Recherche) as one of its key laboratories, and a CNRS $(RI)^2$ project (Recherche à Risque et à Impact) along the same topic is also led by LIMMS since 2024.

In 2024 also, the EURA-LIMMS IRN (CNRS international research network) was started.



In 2025/2026 about 100 people were involved in LIMMS activities including Host Professors (17) and their teams, CNRS researchers (11), engineers (1), JSPS post-doctoral fellows (4), contract based post-doctoral fellows (10), PhD students (4), internships (11), collaborators (37) and administration staff (5).

Organization

LIMMS combines the expertise of French and Japanese scientists in order to explore new scientific domains related to micro and nanotechnologies. Researchers who are recruited by LIMMS are hosted in the Japanese research groups affiliated to LIMMS. The scientific interaction is thus optimal.

LIMMS' structure is organized to handle challenging joint projects. These projects follow the scientific policy promoted by both Directors (CNRS and IIS), and approved by the CNRS Engineering Institute within its interdisciplinary policy with other CNRS Institutes, IIS and JSPS. Each scientific project gathers a LIMMS researcher, the Host Professor heading his/her host lab (The University of Tokyo), and associated lab members (see structure of LIMMS on the figure above).

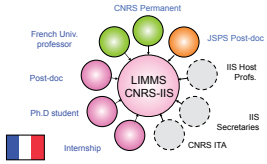
Research costs: salaries of researchers are supported by both CNRS and IIS (CNRS, IIS staff, post-doctorates, PhDs and trainees) or by JSPS, JST, ANR or EU (post-doctorates and PhDs).

The University of Tokyo covers salaries of the group of host professors and provides all technological platforms (1200 m^2 of cleanrooms, biological and biophysics experimental labs, AFM characterization lab, etc.), as well as its operational costs. It is also supporting dedicated administrative staff.

CNRS provides CNRS researchers salaries and the annual research budget, in the framework of a collaboration contract between CNRS and IIS, The University of Tokyo.

Laboratory for Integrated Micro-Mechatronic Systems
LIMMS/CNRS-IIS IRL 2820

LIMMS Recruiting Protocol



1. How to apply to LIMMS/CNRS-IIS (IRL 2820)

a. You have a CNRS researcher position

Step 1:	Step 2:	Step 3:	Step 4:	
(1) Visit to LIMMS for several days (2) Definition of research subject	Validation by LIMMS And by your laboratory	Applying for LIMMS position at INSIS (or institute you belong to)	Approval by National Committee Decision from INSIS	Arrival in Japan
Year N-1	Sep/Oct Year N-1	Autumn Year N-1	Autumn session Year N-1 or Spring session Year N	Sep/Oct Year N

b. You are (associate) professor in French University

Step 1:	Step 2:	Step 3:	Step 4:	
(1) Visit to LIMMS for several days (2) Definition of research subject	Validation by LIMMS And by your University	Applying for "Accueil en délégation" to move to CNRS temporary position	Transfer of the application with agreements to the Regional delegation of CNRS	Arrival in Japan
Year N-1	Sep/Oct Year N-1	Autumn Year N-1	January Year N	Sep N or Feb. N+1

c. You are Ph. D student (to apply for the JSPS Post-doc program)

Step 1:	Step 2	Step 3:		
Positions appear in LIMMS web sites and ABG	Application screening by LIMMS	Application screening by CNRS and JSPS	Expected arrival Sep. 1st – Nov. 30 for Spring Campaign	Arrival in Japan
Spring Campaign				

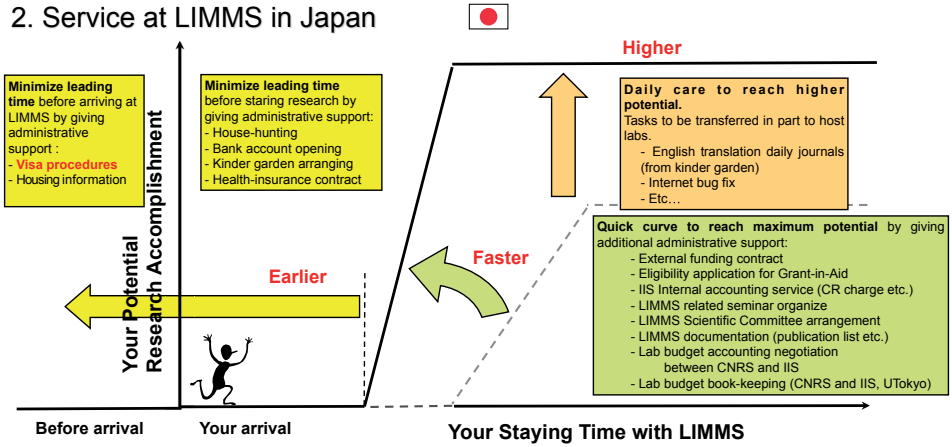
2 Campaigns / year

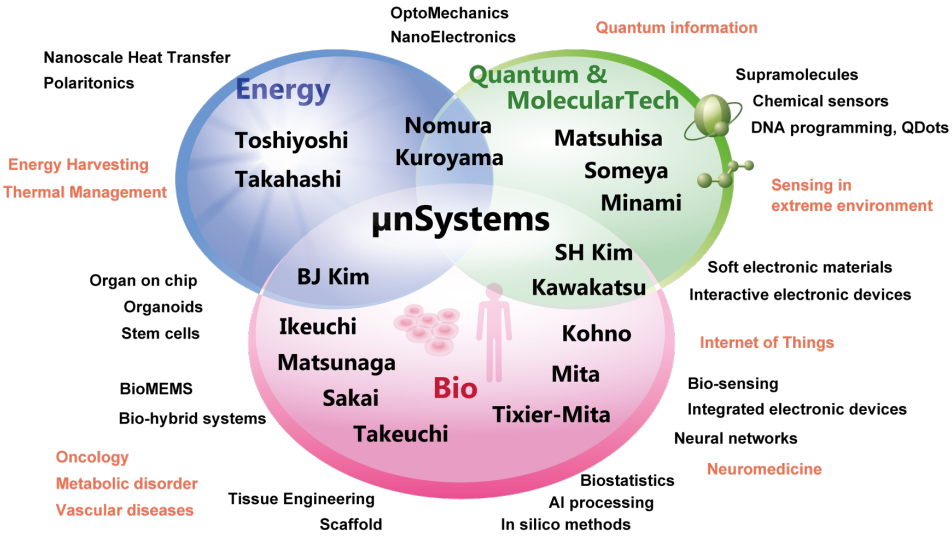
Step 1:	Step 2:	Step 3:	
Positions appear in LIMMS web sites and ABG	Application screening by LIMMS	Application screening by CNRS and JSPS	
Autumn Campaign		Expected arrival April 1 – Sep. 30 for Autumn Campaign	

d. You are student (to apply for Master internship , French doctoral program)

Step 1:	Step 2:	Step 3:	
Position available at LIMMS and Advertisement in web sites (CNRS, LIMMS …)	Application screening by LIMMS	Transfer of the application with approval to CNRS. Recruiting protocols	Arrival in Japan

2. Service at LIMMS in Japan





Scientific Policies

Since 2023, the LIMMS direction has highlighted three general fields of applications in micro and nanotechnologies by proposing three specific research axis:

Energy

Quantum and Molecular Technologies

Bio-engineering

Those three fields are illustrating recent MEMS, BioMEMS and Nanotechnology developments. They reflect the orientations of LIMMS in new technologies related to societal demands.

In Energy axis, LIMMS researchers obtained worldclass results with the development of phononic crystals for heat focusing. LIMMS technologies are at the cutting-edge regarding thermoelectric micro-devices and have confirmed new concepts in thermionic cooling. Interface research programs are also settled to find solutions to power the Internet of Thing (IoT) based on energy harvesters integrated

The Quantum and Molecular Technologies axis is a highly interdisciplinary field that combines cutting research from physics, chemistry, and biology. This axis bridges the two other axes (energy and biology), while also exploring its own unique research questions. At the heart of this axis lies the exploration and integration of quantum technology and molecular technology. Quantum technology is concerned with the use of quantum mechanics to develop new technologies as for instance manipulating the transport of heat, electron or light, while molecular technology deals with the study and manipulation of molecules and their properties. Our research ranges from fundamental endeavor such as single-electron transfer in electrochemistry to the storing of massive data in DNA, the sensing of biomolecules, or the integration of electronic devices into our everyday life with flexible electronics.

The new Bio-engineering axis gathers three themes. Disease treatment via prevention and detection is investigated by developing new devices for diagnosis and vaccine delivery. With a complementary approach, implantable tissues and devices are also key activities.

This branch is related to complex tissues opening to organ modelling where the cellular and even the molecular scale are investigated. Researchers seek to better understand the blood vessel formation, the neuronal communication behaviour and the interaction of the metabolic organs such as liver and pancreas. By studying different organs, LIMMS aims at understanding the role of tissues and especially cell interactions in diseased and healthy tissues.

BioMEMS such as platforms with multi-modal sensors and actuators are developed in LIMMS to help investigating organ behaviour and create biohybrid systems. Biocompatible materials and/or cells are also used to create Bio-robotic systems. A particularity of the Bio axis is the complementary contribution of an international team, SMMIL-E. Its activities are focused on research against cancer, at the interface between BioMEMS and Organ modelling.

SMMiL-E (Seeding Microsystems in Medicine in Lille)

2014 - 2025

The SMMiL-E project was implemented from 2014 to 2025 with the aim to set-up platform of the Institute of Industrial Science of the University of Tokyo (IIS) in the Lille university-hospital area, close to medical teams. First research location of IIS out of Japan, this implantation was involving CNRS, Centre Oscar Lambret and Lille 1 University, as a IRL, International Joint Unit, mirror site of LIMMS/CNRS-IIS (IRL 2820).

Goal : SMMiL-E aims at setting-up and implement a comprehensive research program on BioMEMS against Cancer in a sustainable international high-level collaboration. The project synergizes Bio-MEMS research from LIMMS/CNRS-IIS with research against Cancer performed in Lille under the labeled SIRIC ONCO - Lille program.

2023 ~

EcoLIMMS is a group of researchers who share a commitment for climate change questions, and ask ourselves how we can, as researchers, have a positive impact on the planet. EcoLIMMS was formed in April 2023.

The two main missions established are: (i) act at the laboratory scale, and (ii) organize events to communicate on scientific research and climate change (beyond the lab).

At the lab scale, a monthly newsletter is sent to the lab members to share information on a selected topic, and on specific events related to climate change and environment. The work group has also started working on the greenhouse gas balance of LIMMS which is an interesting tool to evaluate and then optimize our behaviours and practices.

Regarding the events, a crosstalk event was organized in February 2024 with a researcher from Human and Social Sciences and another one from Science and Technology. Other events will be organised over the coming year. This action is in line with the commitments of the CNRS and The University of Tokyo.

CREST (JST) project

2019 - 2026

A CREST project (JST program) was awarded to LIMMS in October 2019 supporting the Energy Harvesting and Management activities. This 6.5 years project (269 Millions Yen) involves two teams, and aims at developing scientific understanding and demonstrators of phonon polariton heat transfer in silicon micro and nanodevices.
This project has been involving four LIMMS researchers (from August 2020).

PEPR MoleculArxiv

2022 - 2029

The dazzling amount of data that humanity generates requires novel solutions for long-term storage. Storing data in the form of DNA, similar to living beings, is a promising option due to its enormous density: 100 g of DNA could in principle store all the data kept in datacenters around the world.

The PEPR MoleculArXiv aims to make of France a key player in DNA storage by involving more than 20 interdisciplinary laboratories from CNRS. LIMMS plays a key role as it is in charge of coordinating and integrating experimental and theoretical progress into a demonstrator that writes information in DNA at a rate of 1 bit per second -100x faster than commercial synthesis in 5 years.

The PEPR will also foster French and European communities and aim to propose a European FET-flagship. Applications will include cold data archiving, marking, calculation, and molecular engineering.

https://pepr-molecularxiv.fr/le-pepr/

PEPR MED-OOC

2024 - 2030

Despite the billions of dollars invested in pharmaceutical research and development, the approval process for new drugs remains lengthy and expensive. The overall success rate of clinical trials for new drugs is only about 10% because traditional cell culture models, animal models) have limited predictive value. In addition, current cell culture models do not mimic in vivo mechanisms and do not easily allow for inter-patient variability, an essential aspect of personalized medicine. The development of in vitro models that faithfully mimic in vivo conditions is therefore clearly one of the cornerstones of future health challenges.

The main objective of the PEPR MED-OOC will be to promote this new generation based on patient-derived cells and tissue precursors such as organoids, with the aim of recapitulating the (patho)physiological reality of the patient's organ, combined with advanced "on-chip" monitoring capabilities.

The budget will support priority flagship projects and specific calls for projects, the creation of open centers for the integration and clinical exploitation of O&OoC, industrial implementation, economic analyses in terms of public health, European synergies and investment in the training of a new generation of O&OoC specialists. In this frame LIMMS is involved in a demonstrator to simulate the cross talk between liver, adipocytes and blood vessel involved in the development of the metabolic syndrome. The project will lenght until 2030 and reinforce synergy between France and Japan

The University of Tokyo Integrated Research Network

The LIMMS KIKO is engaged in a cross disciplinary research for the improvement of the Quality of Life including mental, physical and cultural aspects and addressing societal problems of aging and declining population which developed countries will face, by applying the results of international collaborative research in the Micro-nano interdisciplinary fields such as Nanobiology, µTAS, Silicon Neurons, IoT, and Energy Harvester, etc.

LIMMS KIKO, (LIMMS= “Laboratories for International Research on Multidisciplinary Micro Systems”) was established April 1st 2021 for a period of 10 years and is based on the LIMMS/CNRS-IIS IRL 2820, which has been managed by CNRS and IIS for 25 years as a Japan-France collaborative research center, in order to transcend departmental boundaries and comprehensively bring in the intellectual creativities of the University of Tokyo.

https://kiko.limms-tokyo.org/en/

International Research Network EURA-LIMMS

The EURA-LIMMS network aims to create a Europe-Asia network for the development of innovative technologies in energy, bioengineering, and molecular sciences. The objective is to revive the success of the NAMIS network supported by the CNRS, by adapting the themes to the current research axes of LIMMS. The network will promote the education of students and the exchanges between member teams from: The University of Tokyo, Seoul National University, National Taiwan University, National University of Singapour, EPFL, Helmoltz, Imtek, University of Twente and CNRS.

Contact : N. Clément

LIMMS Key Figures and Collaborations

Since its creation, the LIMMS has welcomed in total **470** members including **52** CNRS researchers, **82** JSPS post-doctorates, **31** CNRS post-doctorates, **14** IIS post-doctorates, **35** PhD students, **10** CNRS research engineers, **82** collaborators, **2** industrial collaborators, **108** internships, **22** administration staff, etc...

Since **2015**, LIMMS has published more than **392** journal papers (including publications in high impact journals such as Nature -/Chemistry, /Biotechnology, /Communications-, NanoLetters, Physical Review Letters...), and more than **317** communications to international conferences.

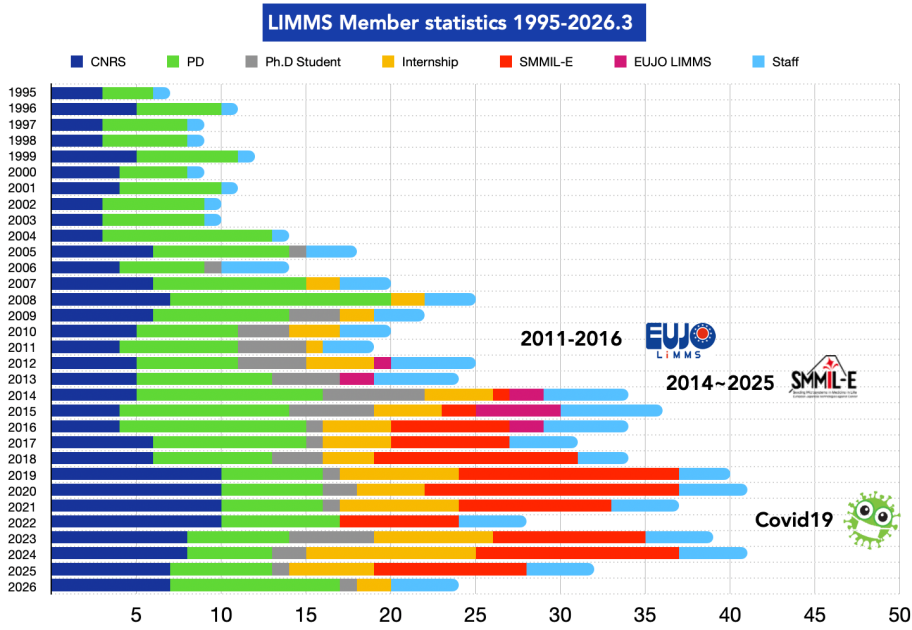
In 2025-2026, our members published **44** journal papers and **15** communications in international conferences.

In this period, LIMMS members have managed **9** grants (6 by JSPS, 1 by JST and 2 by others) and **21** contracts (PEPR, ANR, Region ...).

Former LIMMS members maintain collaborations with Japanese host professors and CNRS laboratories in France (SAKURA programs, PICS and JSPS Bridge).

More than **16** new research teams, often followed by technology exchanges and sharing from LIMMS, were created by former members back in France.

LIMMS has also been pivotal to launching international research networks such as the **CIRMM/IIS** « Center for International Research on Micro nano Mechatronics », the « Global Research Network » of IIS and the **NAMIS** « Nano Micro Systems » linking CNRS to IIS and to prestigious institutions such as EPFL, SNU, VTT, IMTEK.



Events

EURA-LIMMS IRN Summer School in Porquerolles (June 15th ~20th, 2025).

The IRN (International Research Network) EURA-LIMMS of CNRS involving both Asian and European institutions has organized his first event after the 2024 Kick-off in Tokyo. A Summer School was held in Porquerolles, France with about 70 attendees, on the topics of Quantum and Molecular Technologies, Energy Technologies and Biotechnologies for Health.

5th LIMMS-UTokyo/IM2NP-Aix Marseille Univ. Workshop (Nov. 27th~28th, 2025).

The 5th LIMMS-IM2NP workshop has been co-organized with LIMMS and IM2NP in Tokyo. This event continued a long-standing and fruitful collaboration between IM2NP and LIMMS, fostering strong scientific exchanges over the years. Researchers from both institute participated to share their expertise on topics including heat management, photonics, quantum electronics and energy-efficient semiconductor devices. (Co-organizers: Masahiro Nomura and Marc Bescond) ».

Lille/Compiègne Bioengineering Winter School, 2026 School on BioMEMS (6th Ed.) (Feb. 2026)

Lille and Compiegne hosted an international winter school on Bioengineering and BioMEMS in collaboration between LIMMS (University of Tokyo, CNRS), IEMN/OncoLille (CNRS, University of Lille, Centre Oscar Lambret, INSERM, JUNIA) and BMBI (University of Technology of Compiègne, CNRS), from February 9th to 20th, 2026.

This educational event, held for the sixth time, aimed to introduce the main aspects of Bioengineering, Organ on chip and BioMEMS technologies through a multidisciplinary team (15 lectures and visits in Lille and 9 lectures in Compiègne) with backgrounds in biology, clinics and engineering.

7 students from the Institute of Industrial Science and The University of Tokyo, 20 students from the University of Lille, 1 student from JUNIA, 3 students from UTC and 7 PhD from Alliance Sorbonne Universite attended this program and were highly encouraged to join projects between Lille, Compiegne and Tokyo.

In addition to Japanese Professors' lectures, Professor Mita from The University of Tokyo followed and mentored in France some mini projects. Similarly Professor Voican from APHP mentored some projects at the interface of clinic and bioengineering, whereas Professors of Oscard Lambret hospital drived clinical visits. Miniprojects involved French/Japanese mix groups of 4//5 students on organ on chip and microfluidics (such as blood brain barrier, adipose tissue, bone, skin...)

This was also the opportunity for the new LIMMS director, Nicolas Clément, to introduce LIMMS scientific orientation and activities, and for the French students to directly interact with potential future hosting Professors of the University of Tokyo.

Finally, additional financial fundings from Alliance Sorbonne Université (initiative InLife) supported the school in 2026 and will in 2027.

LIMMS/IIS - EPFL Joint Workshop (Mar. 25th-27th, 2026).

The LIMMS/IIS - EPFL Joint Workshop, held in Tokyo from March 25th to 27th, 2026, served as a strategic platform to strengthen scientific cooperation between LIMMS and EPFL, both of which are key partners within the EURALIMMS network. This collaborative event was designed to foster the emergence of bilateral and European research projects, particularly in the fields of micro and nanotechnologies. The program commenced with a welcome reception at the Swiss Embassy in Tokyo, followed by two intensive days of technical sessions featuring prominent talks from EPFL Professors Adrian Ionescu, Nako Nakatsuka, and Edoardo Charbon, as well as Andrada Muntean from the startup Novoviz. In addition to formal presentations, the workshop included poster sessions and laboratory tours. A dedicated technical visit to the NTT Basic Research Laboratories (BRL) further expanded the scope of the event toward high-level industrial partnerships.

30 Years of LIMMS: A Legacy of France-Japan Excellence

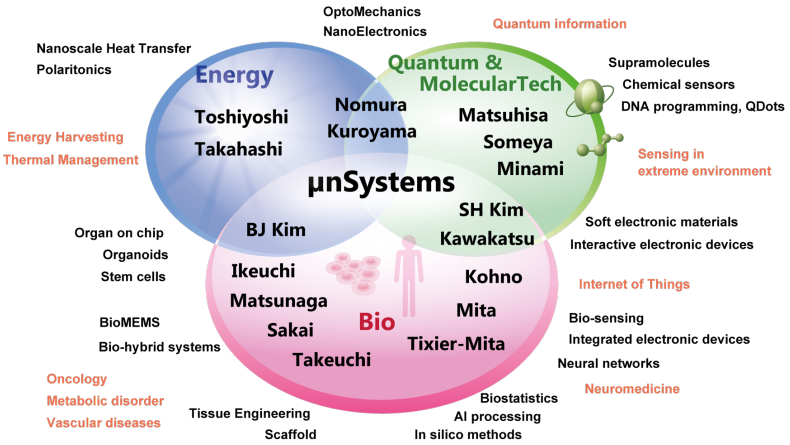
The 2025–2026 academic year marks the 30th anniversary of LIMMS/CNRS-IIS (IRL 2820), celebrated through two landmark events in Paris and Tokyo.

In October 2025, a ceremony at CNRS Headquarters in Paris featured the official signing of the LIMMS renewal agreement by Dr. Antoine Petit (CEO, CNRS) and Prof. Teruo Fujii (President, UTokyo). The event gathered pioneers, including Jean-Jacques Gagnepain and former directors, concluding with a symbolic dinner at Le Procope—the very site where LIMMS was founded three decades ago.

On March 23rd, 2026, the celebration continued at Meiji Kinenkan in Tokyo, focusing on our « Future Vision ». Distinguished guests included President Fujii, IIS Director H. Toshiyoshi, Dr. L. Buchaillot (CNRS), Dr. X. Bressaud (French Embassy), and Ms. Akie Hoshi (JSPS). Following the January 2026 leadership transition, current LIMMS Directors presented a strategic roadmap for our core pillars: Quantum & Molecular, Energy, and Bio technologies.

The event showcased the laboratory's diversity through presentations by LIMMS Host Pr., Researchers, Administrative Manager Ms. Yumi Hirano, CNRS Engineer Dr. L. Jalabert, and our post-docs and PhDs. Founding Director Prof. Emeritus Hiroyuki Fujita concluded the evening with a moving toast.

Host Laboratories



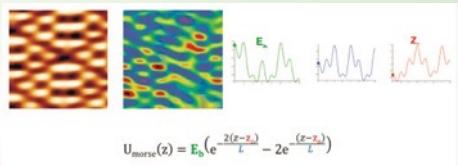
Pr. Yoshiho IKEUCHI

- Neural tissue engineering and brain organoids
- Neuronal morphology and development
- Protein synthesis in neurons
- Human pluropotent stem cell-derived neurons

www.bmce.iis.u-tokyo.ac.jp

Pr. Hideki KAWAKATSU

- Color AFM with chemical contrast
- Force and vibration measurement of reproductive cells
- Quantitative color AFM through Molecular functionalisation of AFM tips

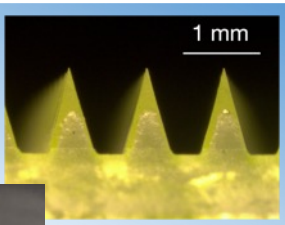


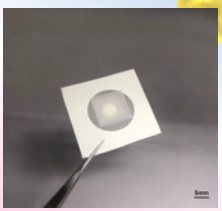
www.inventio.iis.u-tokyo.ac.jp

Host Laboratories

Pr. Beomjoon KIM

- MEMS, Bio-NEMS, Micro/nano patterning, soft lithography
- SAM patterning for cell culturing/bio sensors
- Heat transfer in nano structures, Micro/nano heaters for molecular Engineering
- Microneedle patch for new drug delivery system
- Energy harvesting, power MEMS



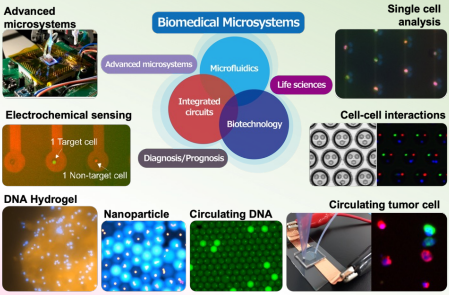


Health monitoring Microneedles patch

www.kimlab.iis.u-tokyo.ac.jp

Associate Pr. Soo Hyeon KIM

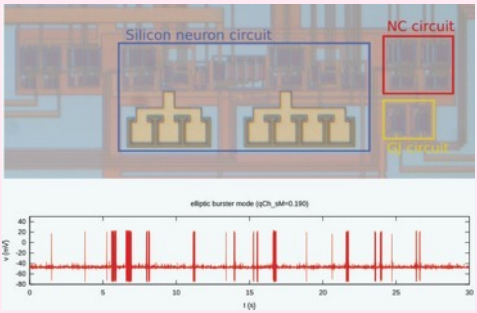
- Single cell analysis
- Single molecule detection
- Biomedical microsystems for liquid biopsy
- 2D flow cytometry
- Electrochemical sensing
- DNA computing



www.shkimlab.iis.u-tokyo.ac.jp

Pr. Takashi KOHNO

- Neuromimetic silicon neuronal network circuits and their application to neuromimetic artificial intelligence
- Architectural design of the neuromimetic computing

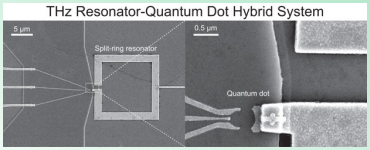


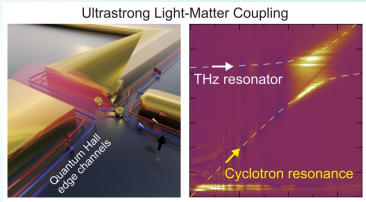
www.neumis.iis.u-tokyo.ac.jp

Host Laboratories

Associate Pr. Kazuyuki KUROYAMA

- Terahertz dynamics of quantum nanostructures for quantum information processing
- Terahertz ultrastrong light-matter coupling

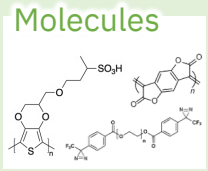




https://www.qnel.iis.u-tokyo.ac.jp/

Associate Pr. Naoji MATSUHISA

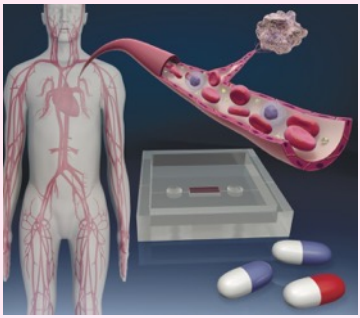
- Stretchable electronics
- Soft materials
- Conducting polymers
- Wearable devices
- Human-computer interfaces



https://www.naojimatsuhisa.com/

Pr. Yukiko MATSUNAGA

- Tissue engineering
- Biomaterials
- In-vitro microvessels model
- Vascular biology

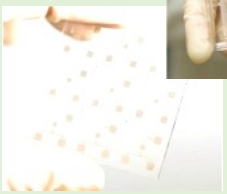


www.matlab.iis.u-tokyo.ac.jp

Host Laboratories

Associate Pr. Tsuyoshi MINAMI

- Organic TFT-based chemical sensors
- Supramolecular sensor arrays



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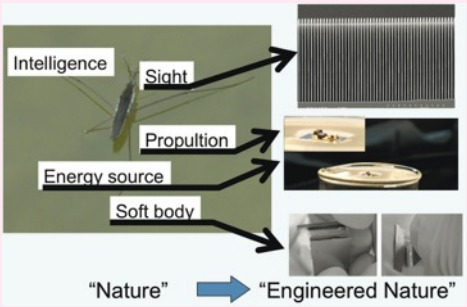
Pr. Yoshio MITA

- Integrated MEMS-VLSI technology
- Nature Engineered Microdevices
- Nano deep 3D MEMS optoelectronic systems
- Autonomous microrobot
- Bio-inspired perception LSI systems



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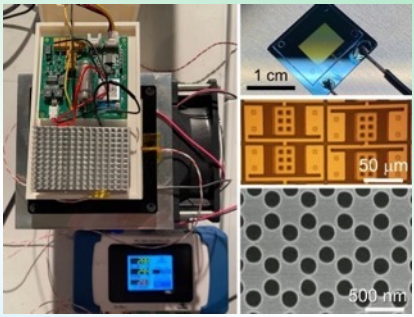
Pr. Masahiro NOMURA

- Physics of nanoscale phonon/heat transport
- Nano-Si thermoelectric energy harvesting
- Quantum transducer via spin-optomechanics



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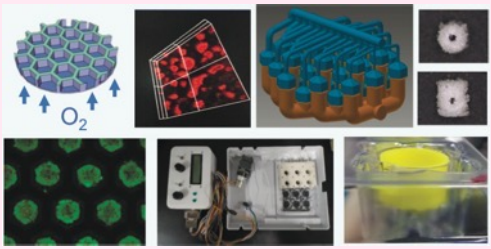
Host Laboratories

Pr. Yasuyuki SAKAI

- Physiological micro cell culture system (MPS) based on microfluidics, micropatterning and hierarchical cellular organization
- 3D microfabrication and biofabrication for engineering of implantable tissues
- High-cell density propagation and differentiation of stem/progenitor cells



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- Flexible electronics using organic transistors
- Large-area sensors and actuators
- Molecular/organic electronics
- Printing technologies for large-area electronics
- Printed MEMS switches for power transmission

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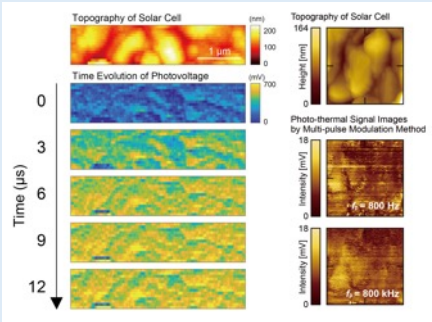
- Multiple analyses of solar cell materials by photo-assisted nanoprobes
- Development of novel measuring methods to improve performance in SPMs
- Analysis of individual fine current paths in CNT-FETs by MFM



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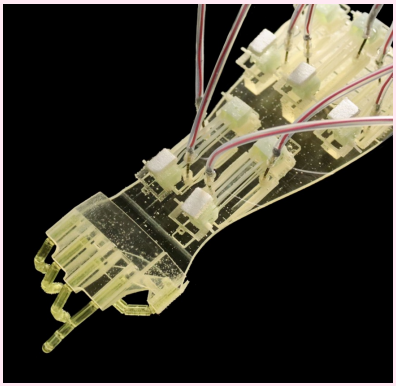
Pr. Shoji TAKEUCHI

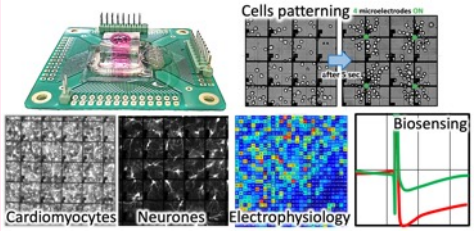
- Biohybrid Robotics
- Cultivated Meat
- Cell-based Sensors
- Organoid on a Chip
- Artificial Cells



www.hybrid.t.u-tokyo.ac.jp

Associate Pr. Agnès TIXIER-MITA

- Thin-Film-Transistor platform for multi-modal bio-sensing
- Real-time biomimetic platform for neuro-cardiac investigations
- Systems for simultaneous optical and electrical measurements on cardiomyocyte cell culture



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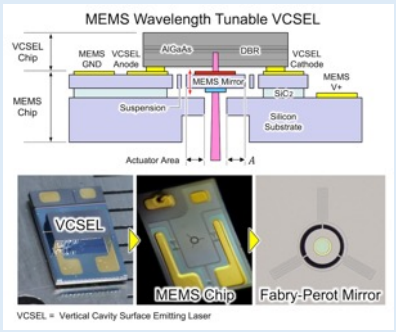
Pr. Hiroshi TOSHIYOSHI

- Optical MEMS
- RF-MEMS
- THz metamaterials
- CMOS-MEMS integration
- Energy harvesters



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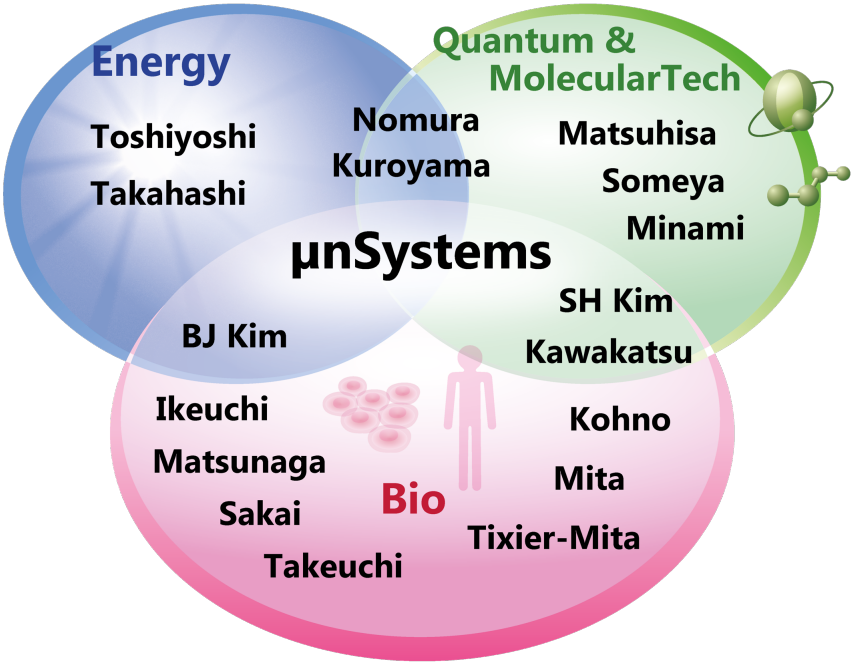
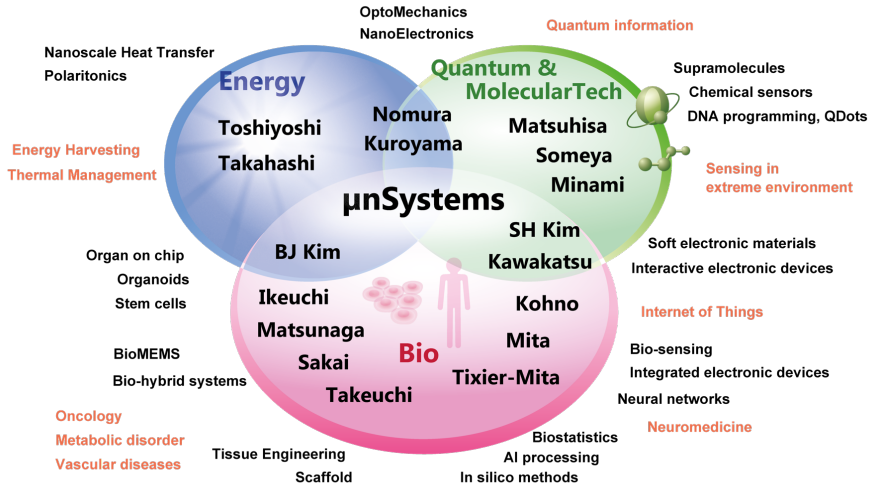
Research Projects

The laboratory operates in three fields, Energy, Quantum and Molecular Technologies, Bio-engineering.

Details about all research projects conducted from April 1st 2025 to the March 31st 2026 will be given in the following part of the booklet.



Energy



Axis leaders : R. Anufriev, M. Nomura

Enhancement of thermal radiation via the hybridization of surface phonon-polaritons and guided modes

Maelie Coral (Nomura Lab)

Keywords: Radiation, Cooling, Nanoscale

Context and Objectives

Surfaces phonon-polaritons (SPhPs) are electromagnetic surface waves generated by the coupling of infrared photons and optical phonons at the interface of polar materials. Even though these evanescent waves have been widely exploited to enhance the cross-plane heat transport in nanocavities (1), recent studies show that they can also enhance significantly the in-plane heat flux emitted by macroscopic cavities. For a vacuum cavity in between two parallel flat plates of SiO2, theory predicts that the maximum enhancement of the radiative heat flux appears for a cavity gap of around 1 cm (2).

Methods

In this work, we aim to provide evidences of this enhancement driven by SPhPs. A theoretical study of the flux in silicon and silica cavities is studied using SCUFF-EM - a software based on the fluctuating surface current (FSC) method for simulating electromagnetic interactions, including thermal radiation. Unlike SiO2, Si does not support the SPhPs propagation and therefore we compare our measurements for Si and SiO2 cavities to provide a proof of concept of the SPhPs contribution. To complete the study, FTIR measurements using an integrating sphere are performed to access the diffuse frequency response of the SPhPs contribution.

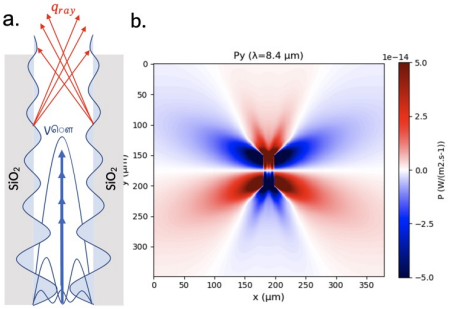


Fig.1.a. Scheme of a vacuum cavity between two identical polar materials supporting the in-plane propagation of SPhPs via cavity modes (blue lines). Classical and Planck radiation (red arrows) adds up to this latter contribution. b. Poynting vector mapping of the cavity effect for SiO2 at 8.4 μm, maximal wavelength of SPhPs propagation. The cavity effect is isolated by dividing the impact of two independent walls.

Results & Perspectives

Use this effect to design SPhP diodes.
Study the influence of cavity size on the field
Investigate regime changes as the distance from the cavity aperture increases

References

[1] S.-A. Biehs and al.: Rev. Mod. Phys. 93, 025009, 2021.
[2] S. Volz and al.: Phys. Rev. Applied 18, L051003, 2022.

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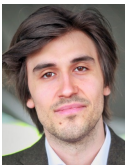
Algorithm-driven design of nanophononic devices for future quantum technologies

Michele Diego (Nomura Lab)



Keywords: Nanophononics, Nano-resonators, Inverse-design

Context and Objectives

Phononic nanodevices operating in the quantum regime represent an emerging field with great potential for quantum hardware technologies, as phonons can couple to a wide range of quantum systems and their short wavelengths enable compact device architectures.

However, different quantum operations require devices with specialized functionalities and, therefore, specific phononic structural designs.

Our research focuses on the experimental implementation of phononic devices obtained through algorithmic optimization methods. By automating the design of these devices, we aim to achieve on-demand optimized performance for a variety of quantum operations [1].

Methods

Fabrication:
- Electron beam lithography
- Nanopatterning
- Reactive ion etching
- NEMS

Characterization:
- Optics (Brillouin / Raman spectroscopy)
- Electro-acoustics (interdigital transducers for generation/detection of acoustic waves)

Design:
- Finite element methods
- Genetic algorithm optimization

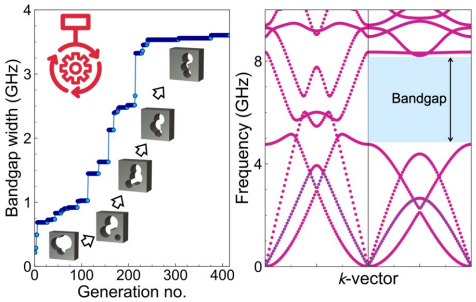


Fig.1. Optimization process of a phononic crystal based on a genetic algorithm design approach (left) to achieve a highly anisotropic bandgap (right).

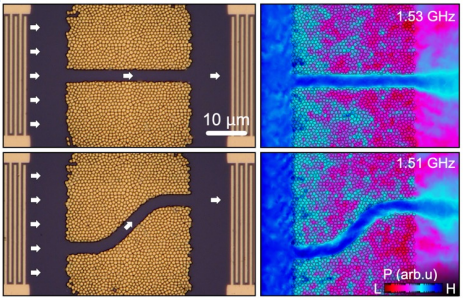


Fig.2. Microscope images (left) and finite element simulations of waveguiding effect (right) induced by nanophononic structure obtained by depositing nano-pillars with a hyperuniform distribution on a piezoelectric substrate.

Results & Perspectives

- Design optimization methods for phononic devices with on-demand phonon dispersion properties [2]

- Hyperuniform structures for broad-band phonon attenuation and waveguiding [3]

References

[1] M.Diego et al., Phys. Rev. Appl., 2024, 21 (6)
[2] M.Diego et al., ACS Nano, 2024, 18 (28)
[3] M.Diego et al., Sci. Adv., 2025, 11 (32)

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Beyond Phonons: Surface Polaritons and Radiative Engineering for Extreme Thermal Control

Georges Hamaoui (Nomura Lab)

Keywords: Surface phonon polaritons, FTIR Spectroscopy, Black Silicon, Infrared emissivity, Thermal interfaces

Context and Objectives

Controlling thermal radiation at high temperature is essential for infrared metrology, thermal management, and advanced energy systems. Commercial cavity blackbodies provide high emissivity (ε ≈ 0.99) but remain bulky and difficult to integrate into compact experimental platforms.

The objective of my work at LIMMS (Nomura Lab) is to develop microstructured Silicon, as a compact, planar, and integrable blackbody reference. The project aims to characterize its emissivity as a function of wavelength, temperature, and angle using high-precision FTIR measurements, and to evaluate its potential as a new radiative standard for infrared systems.

Methods

Spectral emissivity measurements are performed using a FTIR spectrometer. The setup allows direct radiance measurements as well as emissivity extraction by normalization to a certified cavity blackbody from Japan Sensor (ε ≈ 0.99). Measurements are conducted in the 2.5–20 μm range, for different temperatures and incidence angles.

The BSi samples are fabricated in the cleanroom at ESIEE Paris using microstructuring processes optimized to enhance light trapping and radiative absorption. The comparison between spectral radiance and normalized emissivity ensures consistency and robustness of the measurements.

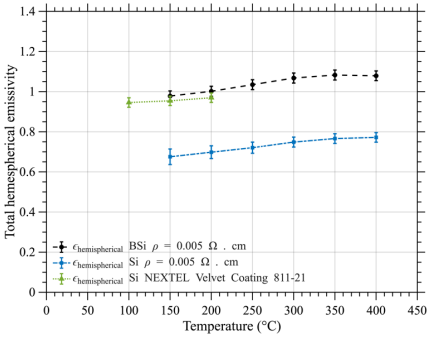

Fig.1. Spectral emissivity of black silicon, flat silicon and flat silicon coated by a NEXTEL black paint normalized to a Japan Sensor cavity blackbody (2.5–20 μm).

Results & Perspectives

The first measurements show that BSi exhibits emissivity values comparable to the commercial cavity reference across the mid-infrared range. At short wavelengths, the measured radiance is even higher than that of the cavity blackbody under identical conditions, confirming the excellent radiative performance of the material.

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Thermal conductivity measurement of spherical fillers for Thermal Interface Materials (TIMs)

Pauline Pradal (Nomura Lab)

Keywords: TIMs, microscale time-domain thermoreflectance, single filler thermal conductivity, FEM, design of experiments (DOE)

Context and Objectives

TIMs rely on conductive fillers whose thermal properties depend on synthesis and post-processing. [1] However, individual spherical fillers have not been yet measured in their as-synthesized state. [2]

We present a simple approach combining µTDTR and FEM simulations to characterize single as-synthesized fillers. Validated on alumina particles with diameters from 4 to 55 µm, this method reliably determines filler thermal conductivity and supports the optimization of TIM design.

Methods

Fabrication:
- -Photolithography
- -Reactive Ion Etching
- -Physical Vapor Deposition

Characterization:
- -Time-domain thermoreflectance
- -Scanning Electron Microscopy

Modeling and Data analysis:
- -Finite Element Method
- -Design of Experiments

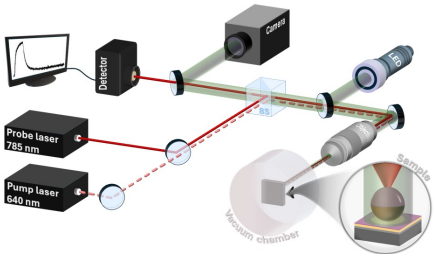

Fig.1. Schematic of the µTDTR setup showing the sample with as-synthesized fillers in a vacuum chamber for thermal decay measurements.

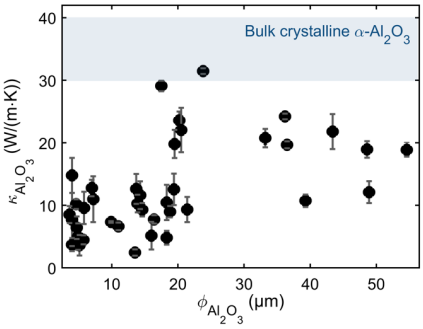

Fig.2. Thermal conductivity of Al_2O_3 fillers measured for different diameters ranging from 4 to 55 µm.

Results & Perspectives

- Simple sample preparation without post-synthesis processing
- Accurate thermal conductivity measurement of individual spherical fillers using µTDTR and FEM, validated by DOE and sensitivity analyses
- Pathway to improved TIM performance

References

[1] Z. Xie et al., Adv. Funct. Mater., 2023, 33, 2214071
[2] M.F. Thompson et al., Appl. Phys. Lett., 2021, 119, 023904

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Phonon properties under confinement in nanostructures and microelectronics

Roman Anufriev (Nomura Lab)

Keywords: Phonons, Dispersion relation, Spectroscopy, Nanoscale

Context and Objectives

Phonon confinement is an important aspect of modern technology, as restricting vibrational modes in one or more dimensions changes properties of phonons, which in turn change acoustic, mechanical, and thermal properties of the material. Thus, understanding phonon confinement is important for various optomechanical devices, sensors, phononic crystals, resonators, and acoustic quantum computers.

Methods

Clean-room nano-fabrication

Characterization:
Brillouin light scattering spectroscopy
Raman spectroscopy

Modeling:
Finite element method
Monte Carlo phonon transport
Fluctuational Electrodynamics

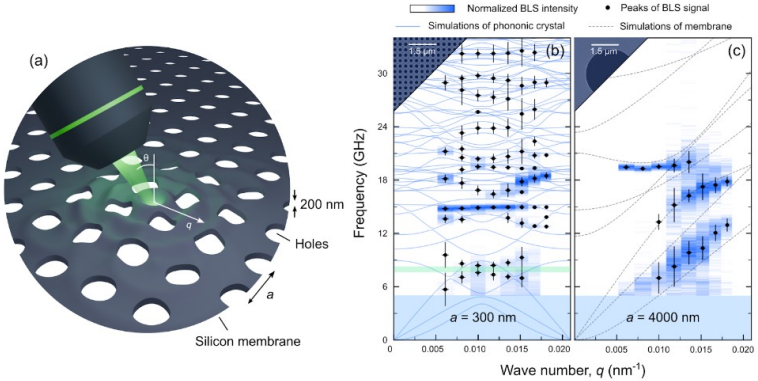

Fig.1. Brillouin light scattering spectroscopy applied to measure phonon dispersion.

Results & Perspectives

Measured phonon properties in a wide range of confined nanostructures and uncovered a fascinating regime of partial confinement. Future measurements will show transitions between 1D, 2D and 3D confinement regimes.

References

[1] R. Anufriev et al. Phys. Rev. Appl., 24 L061001 (2025)

[2] Diego et al., The European Physical Journal Plus Plus 139, 1032 (2024)

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CREST Project: Surface Phonon-Polariton Heat Transfer (2019-2026)

Sebastian Volz (Nomura Lab)

Keywords: Radiation, Cooling, Nanoscale

Context and Objectives

Designing nanoscale heat spreaders in silicon devices.
Investigating a new heat transfer channel based on SPhP in the in-plane direction.
In ultrathin films at high-T, SPhPs are the predominant heat carriers.
We aim at experimentally demonstrating this prediction and then manipulate SPhP by guiding, tunneling, rectifying and focusing.

Methods

Fabrication:
Clean-Room silicon processes.
Characterization:
Time-Domain Thermo-Reflectance;
3 omega; IR Camera and FTIR.
Modeling:
Analytical solution of Maxwell;
Boltzmann and Heat conduction Equations;
Fluctuational Electrodynamics (SCUFF-EM open source code)

Context and Objectives

Demonstrators include:
- Proof of concept
- Focusing and tunneling
- Switching and rectifying
- Trapping

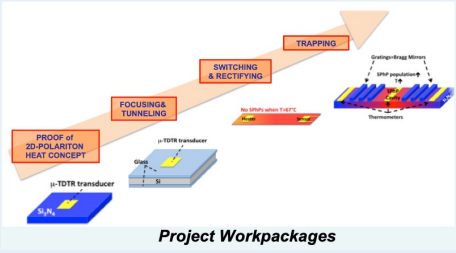

Fig.1. Stages of the CREST Project

Perspectives

Design SPhP Diodes;
Exploiting modulated regimes;
Use SPhPs to control far-field thermal radiation.

References

[1] J Ordonez-Miranda, et al., Phys. Rev. B 111 (19), 195435 (18), 186904, (2025).
[2] J Ordonez-Miranda, Phys. Rev. B 112 (23), 235420, (2025).

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Monte Carlo simulations of phonon and electron transport in thermoelectrics devices

Simon Defradas, Victor Remy, Roman Anufriev (Nomura Lab)

Keywords: Electrons, Phonons, Monte Carlo, Thermoelectrics

Context and Objectives

Thermoelectric energy generators offer conversion of wasted thermal energy into usable electricity. Latest research indicates that nanostructuring, and specifically phononic crystals, is a promising approach to enhance the conversion efficiency. However, the unexpected non-linear impact of nanostructuring on thermoelectric properties is currently poorly understood because of complex behavior of both phonons and electrons in phononic crystals. The objective of this project was to develop a Monte Carlo software capable of simulations of electron and phonon transport in phononic crystals.

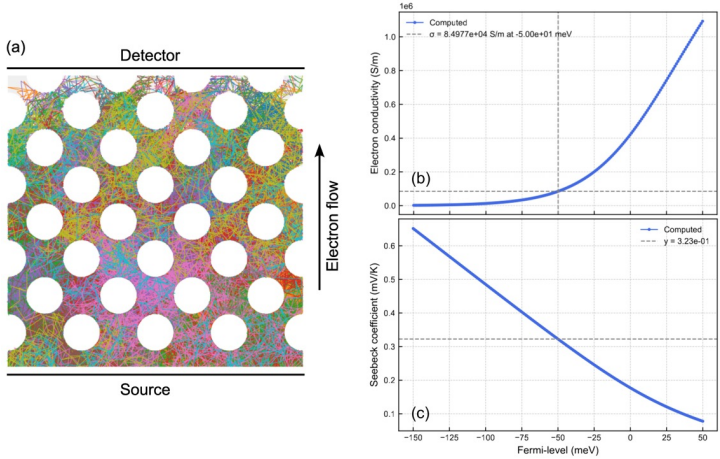

Fig. 1. Monte Carlo simulations of electron transport. (a) Electrons traced through the structure. Obtained (b) electron conductivity and (c) Seebeck coefficient as a function of Fermi level.

Results & Perspectives

We developed the open-source software FreePATHS capable of simulating both phonon and electron transport in thermoelectric generators. Currently, we are applying the simulations to experimental samples fabricated by our colleagues in the laboratory.

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Shaping radiative properties at the microscale in the infrared

Victor Guillemot (Nomura Lab)

Keywords: Microscale radiative heat transfer, near-field electromagnetism, thermal management, phonon-polaritons.

Context and Objectives

Any body at temperature T emits radiative energy through photons. For macroscopic objects, this emission follows Planck's law, resulting in low energy density and weak spectral and spatial coherence.

By structuring matter at the subwavelength scale, these limits can be overcome, enabling unique radiative features and precise spatial and spectral control of the emitted flux.

Such control is crucial for advanced applications in thermal management, sensing, and energy conversion.

Methods

3ω / 2ω measurements of heat transport properties.

Spatially and temporally resolved infrared thermography.

Fourier-transform infrared spectroscopy (FTIR).

Boundary Element Method (BEM) simulations and fluctuational electrodynamics.

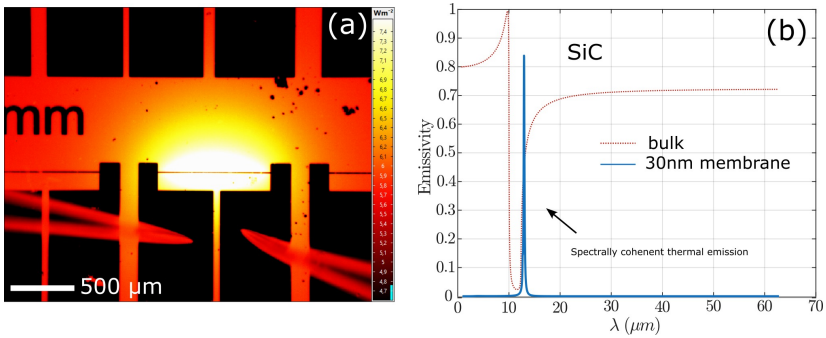

Fig.1 (a) Infrared thermography of a suspended SiC membrane. (b) Emissivity spectrum highlighting spectrally coherent thermal emission from a 30 nm SiC membrane compared to bulk SiC.

Results & Perspectives

Design of coherent emitters with tailored radiative properties through the engineering of material properties and subwavelength structures such as photonic metasurfaces or multilayer systems.

Development of a vacuum thermal imaging platform.

References

[1] V. Guillemot et al. Phys. Rev. Lett., 134, 193801 (2025)

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Ultra-High-Temperature Vacuum Prober for Electrical and Thermal Measurements

Laurent Jalabert (Nomura Lab)

Keywords Thermal Conductivity, Diffusivity, Extreme Temperatures

Context and Objectives

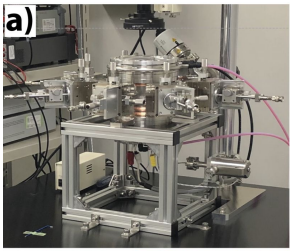
Electrical and thermal measurements at ultra-high temperatures are essential for evaluating the reliability of devices designed to operate in harsh environments. However, most of commercial probers are limited to 800 K and intermittent contact at the highest temperature.

Here, an new vacuum prober operating routinely up to 1200 K, and measuring continuously electrical signals for days or weeks.

Methods

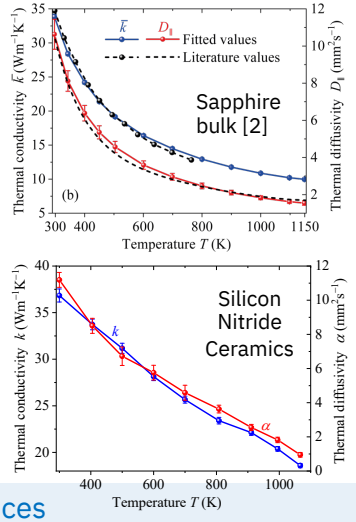
The vacuum machine integrates a Silicon Carbide heater and six probes [2].
A cooling engineering was patented.

We use the 3ω/2ω setup to evaluate the thermal conductivity and diffusivity of materials (bulk, thin film).



Results

We evaluated the linear and non-linear temperature coefficients of resistance of two patterned Cr/Pt micro resistors separated by a distance of 8.83 um. We implement those TCRs in an analytical thermal model [1] for retrieving both the thermal conductivity and diffusivity of a bulk sapphire. Results are in excellent agreement with the literature data.



Perspectives

The setup is suitable for testing sensors, transistors and devices for operating in harsh environment, especially those made of wide bandgap semiconductor and carbon based microsystems.

References

[1] J. Ordonez-Miranda, et al., JAP 133, 205104 (2023).
[2] L. Jalabert et al., Rev.Sci.Instr, 96,8 (2025)

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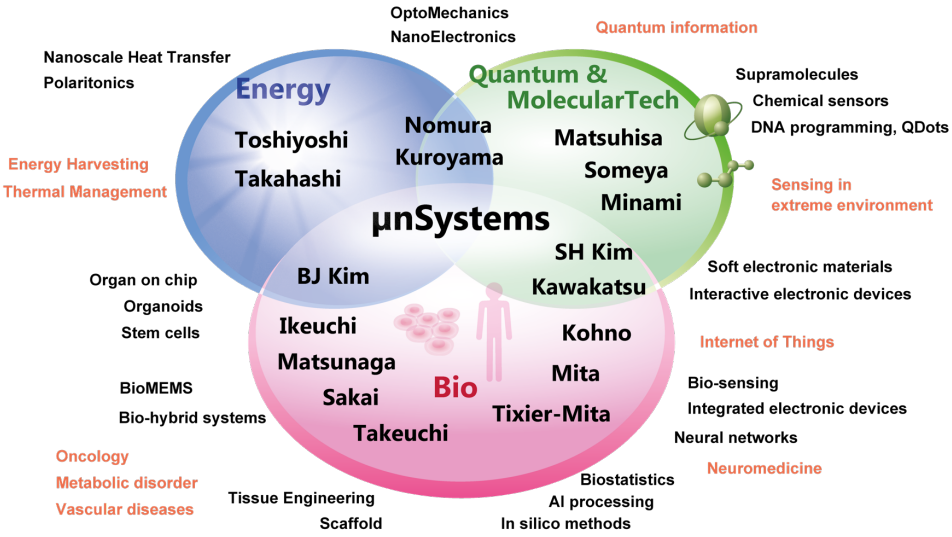
Quantum & Molecular



Axis leaders : A. Baccouche, T. Minami

Computational Design of DNA aptamers for Quantum Bio-Electrochemical Detection

F. Cleri,[1,2] T. Muratov[2]

[1]SH Kim lab, [2]IEMN University of Lille

Keywords: DNA aptamers, cancer proteins, single-electron detection

Context and Objectives

DNA aptamers are fixed on Au electrodes for quantum electrochemical detection of DNA-protein interaction in living cells.

Experimental SELEX techniques for producing DNA aptamers are still today very expensive and difficult.

Machine-learning and AI-based computational tools can be of great help in tailoring the DNA sequence and 3D structures best suited for protein detection.

Methods

- Bidirectional anchored generative transformer model (GPT) using pre-trained protein and DNA sequences, and 3D structures, both at training and inference steps.
- Integration with molecular dynamics simulation of the realistic interactions, in a full-atom model of the quantum bio-electrochemical sensor.

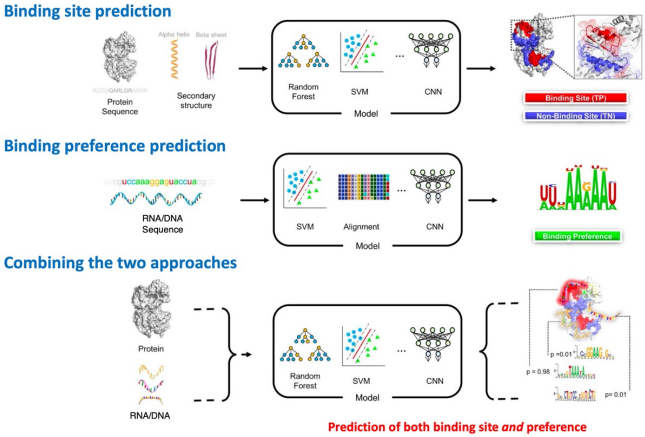


Fig.1. Different paradigms for predicting protein-DNA interaction. Machine learning simultaneously considers the protein and DNA, including their sequence and structural information, to predict best binding sites and chemical binding preference.

Results & Perspectives

Aptamer of single-stranded DNA, with sequences explicitly designed to selectively recognize, e.g., cancer-marker proteins, and carrying a redox species to generate quantum-tunneling current, will be adapted to lab-on-chip devices

References

N. Clement et al. Biosens. Bioelectr. 216, 114643 (2022)

N. Clement et al., ACS Sensors 8, 2921 (2023)

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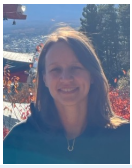
Invisible On-Skin Electrochromic Displays

Séverine De Mulatier (Matsuhisa Lab)



Keywords: Wearable electronics, invisible electronics, wearable displays

Context and Objectives

The Next-generation wearables are expected to be soft, conformable and worn on-skin [1]. They should also remain unconspicuous, visually and by touch, for better acceptance from users [2].
Electrochromic Displays (ECD) are an interesting technology for low-voltage, safe usage of screens directly attached on skin.

Methods

A fully invisible ECD: transparent elastomers for sub- and superstrates, gold-silver nanowires transparent electrodes, and Ru-based electrochromic polymer [4] that switches from purple to transparent.

Superstrate
Conductive electrode
Electrochromic layer
Ion storage layer
Conductive electrode
Substrate

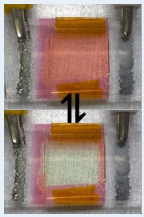
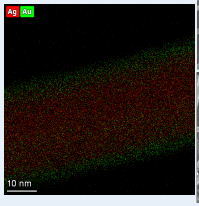


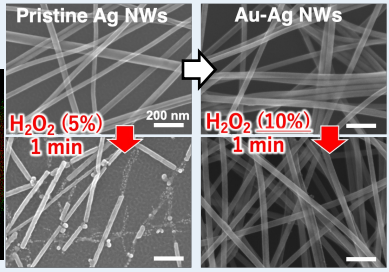
Fig.2. ECD architecture and pictures of color switching in a polyRu-based ECD

Current work

Silver nanowires are easily and non-reversibly oxidized and not suited for electrochemical devices. We protect the nanowires with a thin fold passivation layer of ~ 1.2 nm and showed their improved resistance to chemical oxidation.

Fig.1. ECD based on PEDOT [3]





Perspectives

In addition to soft and conformable mechanical properties, the future display will remain visually imperceptible. This parameter offers new options of integration of wearables technologies into our daily life.

References

[1] Shimura et al., Adv. Electron. Mater. (2023).
[2] Y. Liu et al., Adv. Mater. (2025).
[3] Y. Liu et al. Adv. Mater. Technol. (2023).
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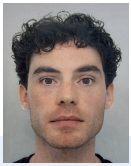
Elastomeric and Organic Semiconductor Nanoparticles for Stretchable Solar Cells

Hugo Laval (Matsuhisa Lab)



Keywords: Organic Photovoltaics, Stretchable, Nanoparticles

Context and Objectives

Stretchable organic photovoltaics (OPV) is needed for wearable applications that demand specific mechanical properties. Particular attention has been given to the development of highly stretchable photoactive layers through different strategies such as blending an elastomer with the organic semiconductors (e-BHJ). [1]

Our project aims to overcome the excessive phase separation that occurs between the two components in the e-BHJ, which can negatively impact the photovoltaic performance, by forming elastomeric nanoparticles (e-BHJ NP) that could confine the phase separation at the nanoparticle scale.

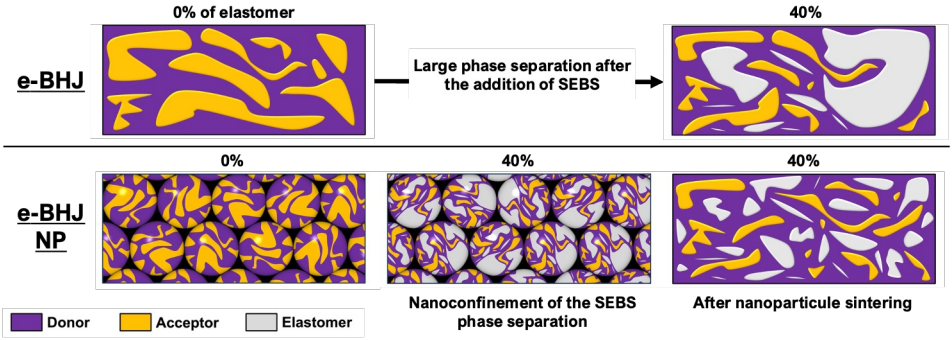


Fig.1. Schematic illustration of the e-BHJ and e-BHJ NP approaches used to form a stretchable elastomeric photoactive layer.

Methods

e-BHJ NPs based on P3HT:PCBM mixed with the elastomer SEBS can be obtained using the miniemulsion method. After film formation, thermal and vapor annealing are used to sinter the nanoparticles.

Results & Perspectives

The nanoconfinement of the phase separation in the e-BHJ NP film was confirmed by AFM (topography and conductive). OPV performance of e-BHJ and e-BHJ NP solar cells are currently being evaluated with varying SEBS wt%.

References

[1] J. Zuo et al. Energy, Environ. Sci., 2025, 18, 6344-6365.

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Redox flow battery characterizations and optimization by spectroelectrochemistry

Stéphane Chevalier (Minami Lab)

Keywords: Heat and Mass Transfers, Imaging, Microfluidic, Electrochemistry

Context and Objectives

Designing optimized redox flow batteries on chip
Investigating the mass and charge transfers in laminar flow

Research hypothesis: In laminar redox flow battery, mass diffusion and charge transfers can be well controlled and measured to optimize their performances.

We aim at experimentally control the mass diffusion and real time monitoring of the electrochemical kinetics by developing new chemical sensors on chip

Context and Objectives

Demonstrators include:

- Proof of concept
- Spectroscopic imaging
- 3D optimization of the channels
- Integration of chemical sensors
- RFB characterization

Perspectives

Proof of concept with integrated sensors

Upscaling the system toward greater power (few W)

Use the characterization technique developed in this project for other electrochemical systems

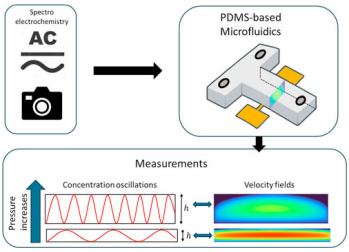

Fig.2. PDMS deformation in microfluidic chip

Methods

Experimental:

Combining microfluidic, electrochemical and imaging methods

Modeling:

Analytical solutions of mass and charge transfers equations;

Mass diffusion, Tafel kinetics and electrostatic equations, COMSOL and Matlab codes

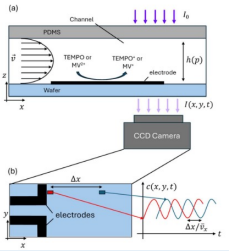

Fig.1 Working principle of velocity measurements

References

1] S. Chevalier, et al., J Power Sources. 655 (2025) 237928.

[2] F. Lavanchy et al., J Electrochem Soc. 173 (2026) 053503.

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Establishing a bridge between quantum devices and electrochemistry

Henri Vo Van Qui (S.H. Kim Lab)

Keywords: Electrochemistry, microfluidics, shot noise, quantum devices, single electron pump

Context and Objectives

Our goal is to bridge quantum devices and electrochemistry. To do so, we have several approaches:

Approach 1: use a formalism from the quantum transport community, adapt it to derive a novel formalism for noise in electrochemical micro systems and prove a universal property of diffusive systems. [1, 2]

Approach 2: study thermal and shot noise in electrochemical systems to experimentally prove the aforementioned theoretical model and help reduce it in electrochemical micro systems.

Approach 3: use an electrochemical device to perform electrochemical single electron pump experiment towards metrology applications. [3]

Results & Perspectives

A novel theoretical model for noise was derived which proposes an analytical formula for the first time.

A proof of concept for an electrochemical single electron pump was achieved.

Room temperature noise in electrochemical systems is better understood which ultimately help to reduce it in cell and ion detection in liquid as well as for energy applications.

Methods

A room temperature noise measurement setup was built, optimized and combined with a microfluidic setup.

Versatile micro-gaped devices were designed and built. They can be used for many applications with minimal modifications.

Custom software programs were designed to control and automatize the different experiments.

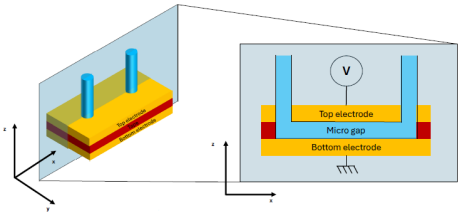

Fig.1. Schematic of the micro gap electrochemical device.

References

[1] Y. Blanter & M. Büttiker, Physics Reports 336, 1–166 (2000)

[2] L. Chen et al. Science 382, 907–911 (2023)

[3] G. Yamahata et al, Nat Commun 5, 5038 (2014)

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LIMMS Internal Project
Bio-electrochimie in High pressure

T. Gabens[1], H. Vo Van Qui[1] ,N. Clement[1], T. Fukuba (JAMSTEC), S.H. Kim[1]

Host Labs: [1]Kim SH lab

Keywords: High pressure, bioelectrochemistry, DNA, Stern layer, electrochemical devices

Context

High pressure alters the organization of water at electrochemical interfaces, affecting the Stern layer and the reorganization energy of electron transfer. In this context, the use of redox-labeled DNA systems translates changes in the interfacial environment into an electrochemical response directly linked to biomolecular motion and the energetic barriers of electron transfer.
High pressure introduces an additional thermodynamic degree of freedom to probe the coupling between interfacial hydration, biomolecular dynamics, and electron transfer energetics.

Objectives

This project aims to perform bioelectrochemical measurements under high pressure using redox-labeled DNA systems to probe pressure-dependent changes in electron transfer kinetics, DNA motion, and interfacial reorganization energy.

Methods

- Bioelectrochemical chips integrating Au and Pt electrodes
- Redox-labeled DNA systems are selected and characterized through electron transfer experiments.
- High-pressure electrochemical experiments by the development of a pressure-compatible device
- Data analysis is performed using Quantum Bioelectrochemistry software (Qbiol)

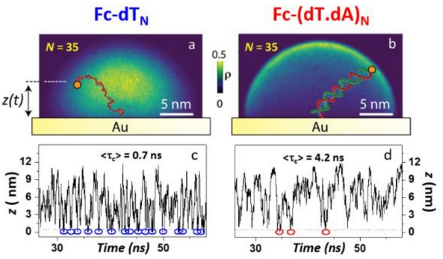

Fig.1. Molecular dynamics simulations of tethered DNA.

Results & Perspectives

Future measurements will explore pressure-dependent electrochemical responses of ferrocene and redox-labeled DNA systems across pressures up to 10 MPa, supported by Qbiol simulations to quantify effects on activation energies and reorganization energy.

References

[1] Zhu et al., Phys. Rev. Applied, 2021
[2]Guan et al., High-pressure electrochemistry, 2020
[3] Z. Zheng et al., Activationless Electron Transfer of Redox-DNA, 2024

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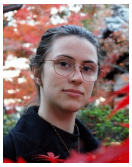
Enzymatic reaction under High pressure

Tiphaine Gabens, Sona Rani Roy (S.H. Kim Lab)



Keywords: High pressure, DNA, Enzymatic kinetics, Enzymatic reaction under high pressure

Context

DNA polymerases operate as molecular machines that replicate genetic information with high efficiency. Their activity relies on finely tuned conformational changes and energetic barriers that govern nucleotide incorporation during the replication process. Enzymatic reactions are inherently sensitive to physicochemical conditions such as temperature, ionic strength, and pressure. Hydrostatic pressure, by modifying protein conformational equilibria and enzyme dynamics, provides a physical parameter that can influence catalytic pathways and reaction kinetics.

Objectives

This study focuses on understanding how hydrostatic pressure influences enzymatic reactions mediated by DNA polymerases and how their catalytic behavior changes under different pressure conditions.

Results & Perspectives

Following the validation of the high-pressure experimental platform, ongoing work focuses on performing replication reactions across a range of controlled pressures. Future studies will extend this approach to multiple polymerases in order to compare how different enzymes respond to pressure

Methods

- Custom high-pressure device combining aluminum plates, 3D-printed components and PDMS elements
- In situ heating of samples under controlled pressure conditions
- PCR amplification, DNA quantification (Qubit) and fragment analysis (Bioanalyzer)
- DNA sequencing for data recovery and analysis of nucleotide incorporation

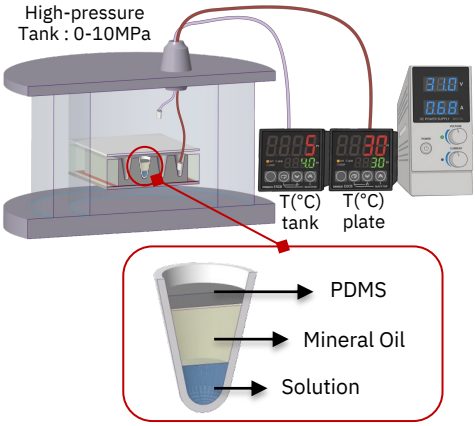


Fig.1. High-Pressure experimental setup.

References

[1] Betancurt et al., Nucleic Acids Research, 2025
[2] Kumar, P., et al. Biotechnology Advances, 2023

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Self assembly of DNA nanoparticles into polymorphic structures

Yannick Tauran (S.H. Kim Lab)

Keywords: Nanoparticles (NP), Smart material, DNA crystal engineering, supramolecular self-assembly, microfluidc platform.

Context and Objectives

Engineering matter at the nanoscale is crucial to extend the unique physico-chemical properties of nanoparticles to larger structures [1]. The implementation of DNA for designer materials has shown unmatched advantages (programmability, directional interaction, responsivity) [2].

Methods

We used a high throughput microfluidic platform [3] to characterize the thermodynamic parameters of the DNA NP self-organization into different morphologies (liquid, gel, glass) [4].

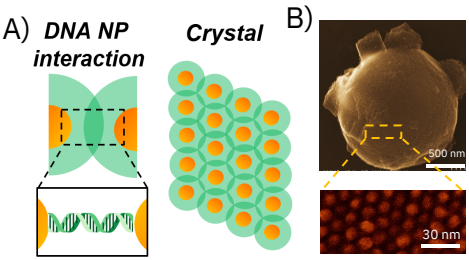

Fig 1. A) Scheme of self assembled DNA NP into lattice. B) Electronic images of DNA gold NP self assembled into micro crystal (top) through lattices (bottom)

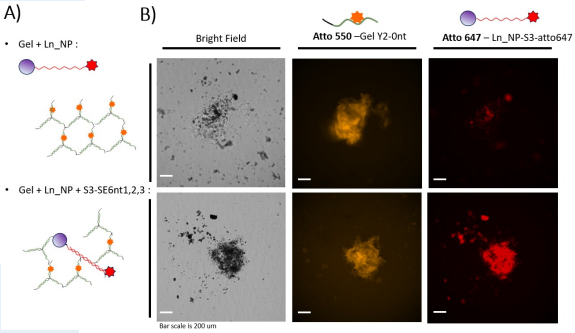

Fig.2 A) Scheme showing before (top) and after (bottom) capture of DNA lanthanide nanoparticles by DNA gel.
B) Bright field and fluorescent image of DNA lanthanide nanoparticles in red before (top) and after capture (bottom) by DNA gel in orange.

Results & Perspectives

- Made a phase diagram of DNA gold NP into different morphologies such as crystal (Figure 1), gel or glass.
- Proposed a model to explain the transition of phases.
- Extended the study to Lanthanide Nanoparticles captured by DNA gel (Figure 2).
- Applications are expected in diagnosis, data storage, etc.

References

[1] Y. Tauran et.al., J. Nanosci. Nanotechnol. 2015
[2] C.R. Laramy et.al., Nat. Rev. Mats. 2019
[3] A. Genot et.al., Nat. Chem. 2016
[4] N. Lobato-Dauzier et.al., Nat. Chem. Eng. 2024

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Work in the frame of IRP CNRS supraDNA

Controllable Reconfiguration of DNA Nanostar Hydrogel Networks via Sticky-End Ligation

Audrey Cochard (S.H. Kim Lab)

Keywords: DNA hydrogels; Biomaterials; Cell culture.

Context and Objectives

DNA nanostar hydrogels [1] hold great promise as biomaterials, but their mechanical properties and nuclease susceptibility limit their use. This project aimed to control the network architecture of DNA nanostar hydrogels using sticky-end ligation as a post-assembly strategy. By tuning the fraction of phosphorylated strands (from P0 to P100), we sought to modulate hydrogel stability and resistance to nuclease. Ultimately, the goal is to develop DNA-based biomaterials with programmable mechanical and biological properties for 3D cell culture.

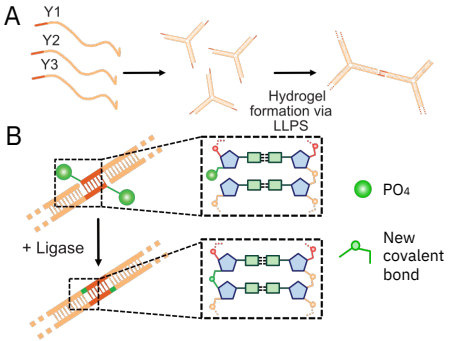

Fig.1: Formation and ligation of DNA nanostar hydrogel. A. Formation via liquid-liquid phase separation. B. Ligation and creation of new covalent bonds.

Results & Perspectives

Sticky-end ligation strongly improved gel integrity and nuclease resistance, while remaining compatible with 3D cell culture (Fig. 2) [2]. This strategy enables post-assembly tuning of DNA hydrogels. Future work could focus on biofunctionalization studies.

Methods

DNA nanostar hydrogels were assembled from Y-shaped motifs bearing complementary sticky ends, with controlled phosphorylation levels (Fig. 1). After gel formation, samples were treated with T4 DNA ligase for defined times to induce covalent crosslinking. Gel properties were evaluated by thermal stability, nuclease degradation assays, handling and 3D printing tests, and proof-of-concept 3D cell culture (Fig. 2).

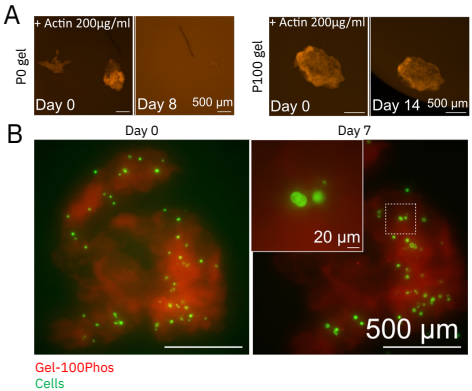

Fig.2: Impact of ligation on DNA hydrogels and applications. A. Unligated (left) and ligated (right) hydrogels in serum-supplemented culture medium. B. Cell culture in a ligated DNA hydrogel.

References

[1] Y. Sato et al. Sci. Adv. 2020
[2] A. Cochard et al. Appl. Mater. Today 2026

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Mechanical and structural analysis of DNA nanostar hydrogels

Hajar Ajiyel (S.H. Kim Lab)

Keywords: Soft matter, Rheology, Calorimetry, Hydrogels, DNA Nanotechnology, DNA sequencing

Context and Objectives

The sequence of nucleic acids can be designed to program self-assembly into a multitude of forms, such as DNA hydrogels.

Their study has focused on their formation and not so much on the thermodynamic and rheological properties with relation to the sequence design.

Therefore, we aim at linking the various mechanical and structural characteristics of the DNA hydrogel to its design, and make a global study at different scales. Applications of DNA hydrogels are anticipated in many fields; in therapeutics, biosensing, etc [1].

Methods

Design DNA sequences that will assemble into a hydrogel with prescribed properties

Determine the phase behaviour of the hydrogel

Test the mechanical properties of the resulting hydrogel with dynamic light scattering

Study the nanoscale structure using DNA nanopore sequencing

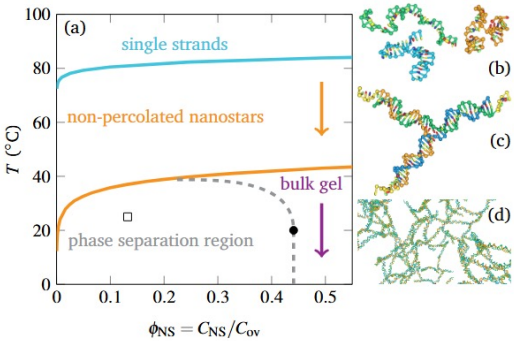

Fig.1. Phase diagram of Y16SE6 Y-shaped nanostar hydrogel.

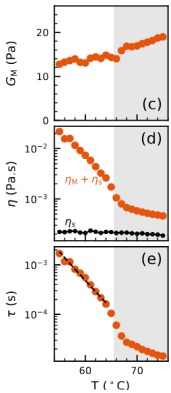

Fig.2. Mechanical properties of Y16SE6 hydrogel at 1mM extracted from DLS experimental data.

Results & Perspectives

DNA nanostar hydrogels are viscoelastic materials, with characteristic timescales that vary across 6 orders of magnitude. Elasticity emerges at high temperatures during formation of the hydrogel.

References

[1] F. Li et.al., Progress in Polymer Science. 2019

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DEVILISH: Dynamics of light energy harvesting and exciton transport in DNA-templated dye networks inspired by photosynthesis

Hajar Ajiyel (S.H. Kim Lab)

Keywords: DNA Nanotechnology, Fluorescence, Exciton transport

Context and Objectives

Photosynthesis relies on light-harvesting systems where networks of chromophores absorb light and transport excitons efficiently to a reaction centre, a process partly enabled by quantum coherence.

Replicating this behavior requires precise control of chromophore arrangement; DNA-based assemblies and dye-loaded polymeric nanoparticles are promising approaches for building artificial light-harvesting systems [1]. We aim to evaluate the quantum dynamics of excitons within innovative LHSs constructed from DNA.

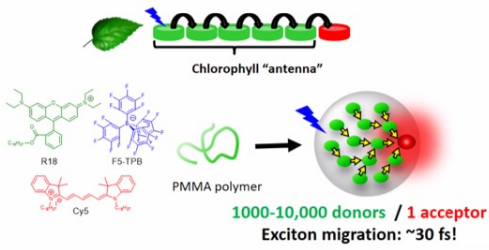

Fig.1. Exciton transport in nanoparticles showing an antenna effect [2]

Results & Perspectives

Design new DNA structures with larger dye linear density

Study exciton transport in these DNA structures and show antenna effect

Methods

Design DNA structures with well-placed fluorophores

Test the assembly and formation of the structures with DNA technology methods

Measure the fluorescence transport in DNA structures using a fluorescence spectrophotometer

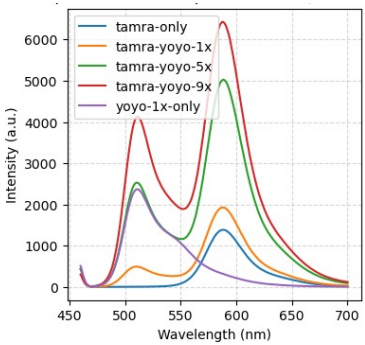

Fig.2. FRET transport in DNA duplex using DNA intercalator, emission spectra with excitation wavelength at 450nm

References

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PEPR MoleculArXiv (2022-2033): Massive Data Storage on DNA and Artificial polymer

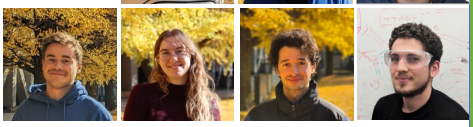
Anthony Genot, Nicolas Clément, Alexandre Baccouche, Paul Bruand, Audrey Cochard, Sona Rani Roy, Yannick Tauran, Léa Cahuzac, Elias Boudjella, Adrien Rey
(S.H. Kim Lab)

Keywords: DNA data storage, DNA synthesis, DNA sequencing, microfluidic platform, electrochemistry

Context

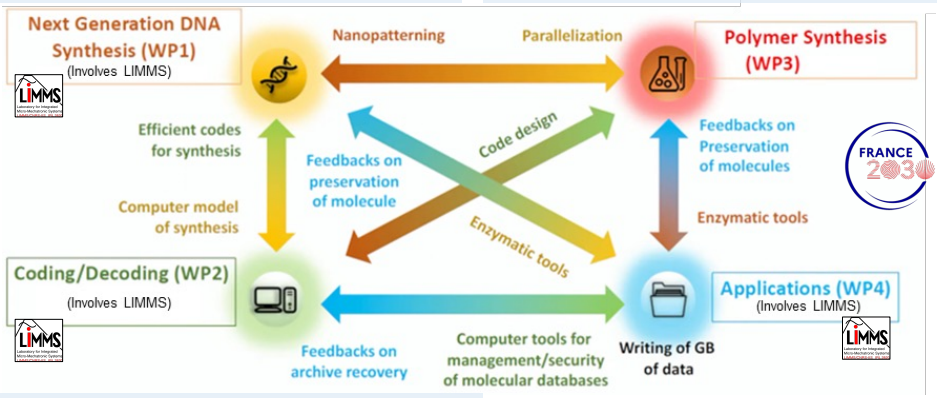
Global data production is exploding (prediction of 1 YB = 10^{24} bytes every year by 2030 [1]), but traditional storage (electronic, magnetic, optical) lacks density and durability. DNA offers ultra-dense and stable storage, but high costs and slow synthesis remain major barriers [2].

In total, 27 scientific units are involved in the project, in France and in Japan (LIMMS). The project consists of 4 interconnected working packages (WP) explained below.



Objectives

- Innovative enzymatic DNA synthesis (WP1)
- Alternative synthesis based on Next-Generation Sequencing (WP4)
- Development of DNA data storage methods & enhanced random access (WP2 & 4)
- End-to-end Integration in microfluidic chip for high throughput parallelization (WP1)



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CalcADN: Computing with data stored in DNA

Daisy Hales & Emma Brix (S.H. Kim lab)

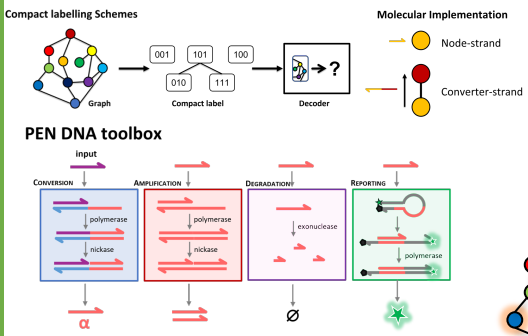
Keywords: DNA computing, molecular programming, Microfluidics, compact labellling schemes

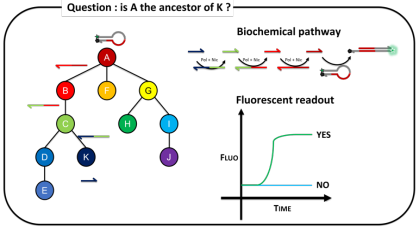
Context and Objectives

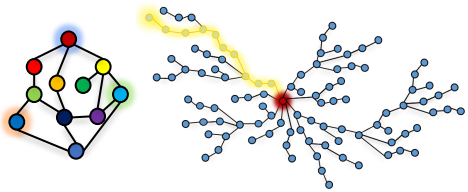
DNA-based data storage is a promising medium for its unparalleled density and durability, yet its computational potential remains underdeveloped. The calcADN project aims to design the first DNA computer capable of executing algorithms directly on DNA-encoded data, pushing the limits of DNA reaction networks from tens to thousands of strands. This breakthrough could enable molecular computation for complex, real-world data analysis.

Methods

Molecular programs are designed using the PEN toolbox [1] to implement DNA-based computation.
Novel fluorescent reporting strategies are developed for real-time monitoring of circuit dynamics.
Microfluidic compartmentalization enables controlled scale-up and parallelized testing of molecular networks [2].







Common ancestry Scale-up: 100 nodes

Results & Perspectives

First functional DNA-based computation trees with 10 nodes have been successfully implemented.
Ongoing work focuses on scaling up to 100-node trees, while investigating sequence design constraints, topological effects, and their integration with population-level protocols for distributed molecular computation.

References

[1] Montagne et al., Nat. Comm., 2016
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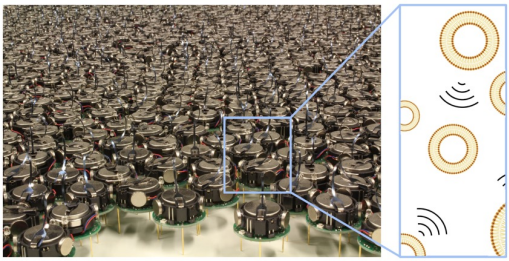
Cell-like robot swarm: encapsulating molecular programming into Giant Unilamellar Vesicles (GUV)

Elouan Julien (S.H. Kim lab)

Keywords: robot swarm, DNA computing, synthetic cells, membrane, giant unilamellar vesicle, microfluidic platform

Context and Objectives

Cell-scaled logic units present a promising platform for clinical applications, such as targeted drug delivery. However, engineering complex behaviors in individual units at this scale is challenging [1].
By combining basic individual behaviors with cell-to-cell interactions, it becomes possible to implement swarm algorithms in cell-like robots, enabling programmable and adaptive micro-systems [2].
Additionally, these artificial cells serve as a model to study the emergence of early lifeforms, offering insights in the fundamental principles of biological organization.



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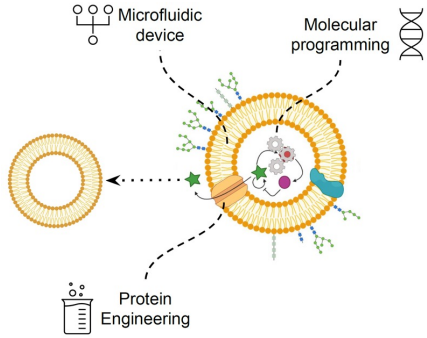

Methods

There are two main axis for this project:
- GUVs with lipid bilayer membranes are created for encapsulation.
- DNA-based computation is implemented inside vesicles to process inputs and outputs.

The production of GUVs with controlled, varying contents is achieved using custom microfluidic devices [3].

To enable communication between GUVs and their environment, specialized membrane proteins are integrated, facilitating interaction with neighboring vesicles.

References

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Engineering synthetic cells for selective CTC capture and in situ analysis

Alexandre Baccouche (S.H. Kim lab)

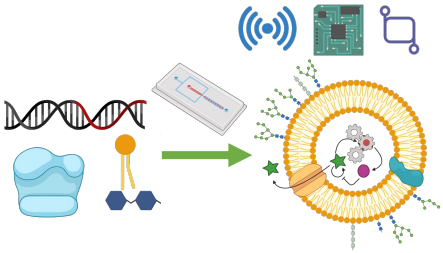
Keywords: synthetic biology, microfluidics, molecular programming

Context and Objectives

Cell-cell communication underpins biological systems, yet engineering synthetic cells to interact precisely with natural cells remains a key challenge in synthetic biology.
This project aims at developing microfluidic-generated synthetic cells tailored to selectively capture and detect circulating tumor cells (CTCs) in blood. By leveraging biomimetic micro-actuators, we aim to enable high-efficiency, high-precision in vitro cancer diagnostics for early metastasis detection and personalized treatment monitoring.

Methods

We engineer existing microfluidic methods for high-throughput synthetic cell generation[1], while integrating custom molecular programs [2] to Cell-Free Protein Synthesis systems [3], enabling dynamic intracellular signaling and controlled metabolic functions in hybrid cellular systems



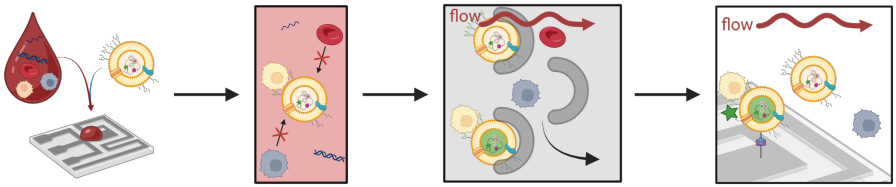


Fig. 1. WorkflowThe SynC and blood are mixed and CTC are recognized selectively by the SynC with high efficiency and dimers trapped on the chip. The molecular program detects the cognate CTC and conditionally release surface binding receptors. Inactive SynC are released, and only the activated SynC attach to the catch surface.

Results & Perspectives

The microfluidic platform for synthetic cell generation is operational. Next steps include designing programmable surface receptors for selective CTC binding and developing fluorescent signaling to enable real-time detection in liquid biopsies.

References

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[2] Gines et al., Nat. Comm., 2016.
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In Memoriam : Anthony Genot (1982–2025)

T.Fujii lab, S.H. Kim lab

Keywords: DNA computing, molecular programming, microfluidics

A graduate of École Polytechnique and a doctorate holder from the University of Oxford, Anthony joined the LIMMS laboratory (CNRS/University of Tokyo) in 2011 as a postdoctoral researcher in the team of Yannick Rondelez and Professor Fujii. After a period at LAAS in 2013, he was recruited as a CNRS research scientist, returning to LIMMS, this time as scientific lead.

His research, focused on DNA computing, flourished at a rapid pace, driven by a deeply innovative ambition. A key contributor to the PEPR MoleculArXiv program, he combined scientific rigor with technological imagination, opening new horizons in the manipulation and programming of matter at the molecular scale.

The year 2024 marked a turning point: at 42, Anthony was awarded the CNRS Bronze Medal, promoted to Research Director, and appointed coordinator of one of the twelve flagship $(RI)^2$ projects of the CNRS. With this momentum, he confirmed a rare quality: that of an architect of national synergies, capable of connecting disciplines, teams, and ideas to bring bold visions to life.

In France as in Japan, many researchers who had the privilege of working with him now feel the loss of a guiding light. He embodied a form of active excellence, equally at ease leading a team that was like a second family to him, as he was in pursuing the grand ambitions of future science.

Anthony Genot exemplified with rare clarity, the ideal of a CNRS researcher: a brilliant and free intellect, a mind in perpetual motion, driven by insatiable curiosity and a deep sense of humanity, qualities that are the strength and uniqueness of our institution.

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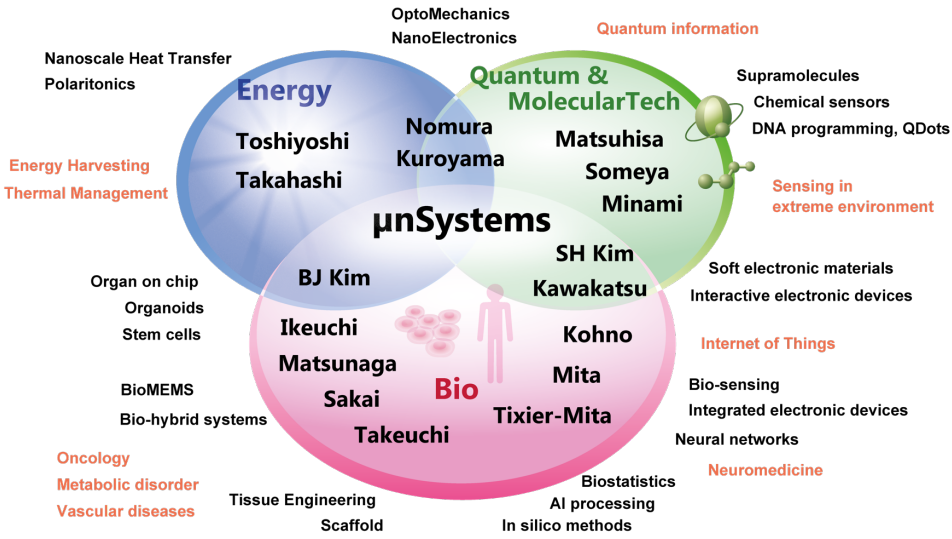
Bio-engineering



Axis leaders : E. Leclerc, Y. Ikeuchi

Emergent Dynamics in Modular Brain Organoid Networks Connected by Axon Bundles

Tomoya Duenki (Ikeuchi Lab)

Keywords: Neuroengineering, brain organoids, optogenetics

Context and Objectives

Limited access to living human brain tissue has hindered direct study of its mechanisms. Recent advances have led to the generation of brain organoids, which are lab-grown miniature brain-like tissues that can recapitulate key structural and functional features of the brain. Yet, individual organoids lack long-range and inter-regional connectivity. Our work aims to overcome this limitation by constructing connected organoid networks that models such connections in vitro.

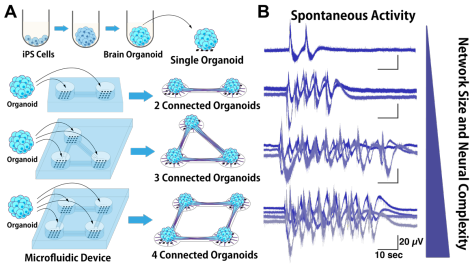


Fig.1. (A) Organoids can be connected using microfluidic devices. (B) Neural Activity increases with more connected organoids.

Results & Perspectives

Multiple organoids can be connected, expanding network size and increasing the complexity of neural activity. Optogenetic stimulation can further modulate the activity, leading to more frequent reappearance of the activated patterns. This study provides a basis for building more complex and physiologically relevant tissues in vitro to explore brain function and potential therapies.

Methods

Microfluidic devices were employed to guide axonal growth between brain organoids, enabling the formation of inter-organoid connections among two, three, or four organoids. These connected organoids were cultured on multielectrode arrays (MEAs) to record neuronal activity and investigate how inter-organoid connectivity shapes network dynamics. Moreover, defined optogenetic activation sequences were delivered over a 12-hour period to evaluate evoked neuronal responses and resulting network-level activity changes upon repetitive long-term stimulation of the network.

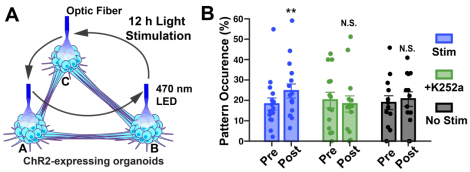


Fig.2. Stimulation of specific sequence for 12h will increase the occurrence of the stimulated pattern in the activity. This increase cannot be observed in presence of a drug or if no stimulation is applied.

References

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Neuro-cardiac in-vitro system for real-time multi-modal investigations.

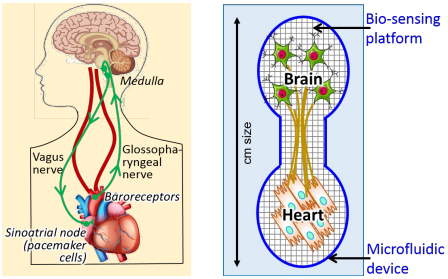
Gauthier Signoret, Ethan Sonderer (Tixier-Mita Lab)

Keywords: Neuro-cardiac, Microfluidic, Multimodal sensing, Electrophysiology.

Context and Objectives

Cardiovascular disease (CVD) is the first cause of death in the world and involves the neuro-cardiac axis. Reproducing the neuro-cardiac axis in in-vitro permits investigations in a controlled environment.

This project aims at developing a microfluidic platform with multi-modal sensors integration for neuro-cardiac investigation. Microfluidic devices were designed and fabricated. Then they were attached to the bio-sensing platform and cell culture were successfully achieved.



a) *b)*

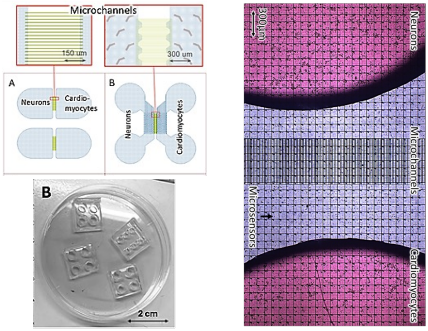
Fig.1. a) The human brain-heart system closed-loop interactions. b) In-vitro microfluidic sensing platform.

Results & Perspectives

Microfluidic devices were designed and fabricated. They were attached to the bio-sensing platform and cell culture were successfully achieved [2]. Next step will validate the neuro-cardiac co-culture, and electrophysiology measurement will follow.

Methods

The microfluidic device will welcome neurons and cardiomyocyte cells co-culture. It is designed to support spatially organized co-cultures and controlled biochemical communication between cell populations [1]. So, both cultures will be separated by microchannels which will permit the axons of neurons to reach cardiomyocytes, while dimensions prevent cells body to reach the other culture.



a) *b)*

Fig.2. a) Top: Design of the microfluidic devices. Bottom: fabricated microfluidic devices. b) Microfluidic device A placed on a bio-sensing platform, with cells cultures.

References

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Development of a Biohybrid Platform to investigate the Neuro-cardiac System

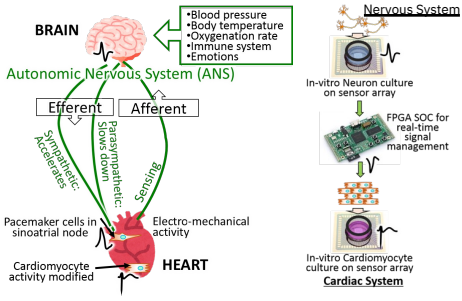
Nathan Dagoury, Quentin Miane,
Léo Delmas, Pierre-Marie Portal (Tixier-Mita Lab)

Keywords: Biohybrid, FPGA, Cardiomyocyte, Real-time stimulation

Context and Objectives

Cardiovascular disease (CVD) is the first cause of death in the world and involves the neuro-cardiac axis [1]. Reproducing the neuro-cardiac axis in in-vitro permits investigations in a controlled environment.

This project aims at developing an electronic platform that reproduces and analyze the interactions between the neurons and cardiomyocytes in real-time. The final goal is to realize a biohybrid model to study more easily neuro-cardiac diseases and search for new therapies.



a) b)

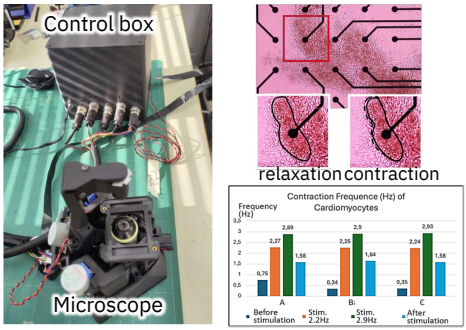
Fig.1. a) Details of the neuro-cardiac axis. b) Bio-mimetic hybrid neuro-cardiac system for the efferent path.

Results & Perspectives

A 3D printed microscope was fabricated in a way to allow simultaneous electrical stimulation and optical observation [2]. Next step will connect the FPGA to sense external information like neurons activity and adapt the stimulation accordingly.

Methods

The contraction of cardiomyocyte cell culture is controlled by an FPGA circuit which plays the role of a pacemaker. It sends biomimetic electrical stimulations towards the cells and adjusts the frequency according to external events. The cardiomyocyte cells are stimulated electrically and respond by contraction. Their optical observation gives information on beating amplitude and frequency.



a) b)

Fig.2. a) 3D printed microscope and control box to manage: microscope, biomimetic stimulation with FPGA, optical observation of contraction. b) Top: cardiomyocyte cells. Bottom: results of contraction.

References

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[2] Tixier-Mita et al., DTDA'2025, Sendai, 2026.

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SOI-CMOS microelectrode array with semi-transparent electrodes for extracellular recording and investigation of cardiomyocytes

Anne-Claire Eiler (Mita Lab)

Keywords: CMOS, silicon on insulator (SOI), microelectrode array (MEA)

Context and Objectives

Development and fabrication of a large-scale integrated (LSI) microchip for recording extracellular electrophysiological signals from bioelectric cells:
- array of 20 x 40 electrodes
- electrode size: 44.0 µm x 36.4 µm
- pitch: 51 µm (~385 electrodes/mm^2)

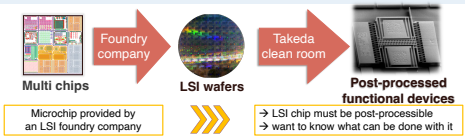

Fig.1. Flow of design, fabrication, and post-processing of microchips

Methods

The microchip is post-processed in a clean room environment, packaged on a PCB, with a PDMS chamber placed on top.

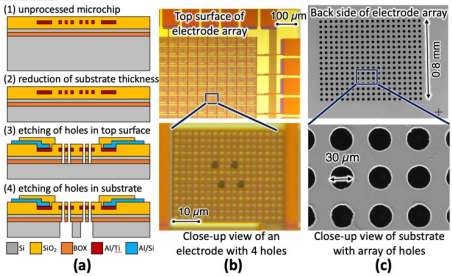

Fig.2. Method: (a) post-processing flow; (b) 2 µm holes in semi-transparent electrode; (c) 30 µm holes behind electrodes in substrate

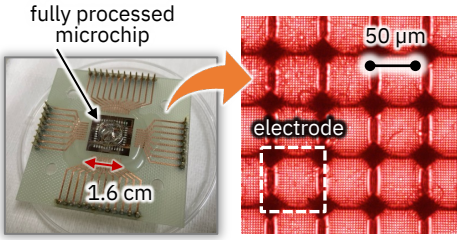

Fig.4. Results: a) finalized CMOS MEA bonded onto PCB with PDMS chamber; b) photo of the cardiomyocyte culture on the electrode array on day 3

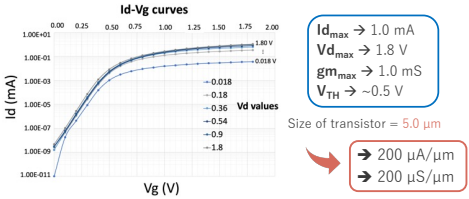

Fig.3. Electrical characterization: drain current vs gate voltage with logarithmic scale, and electrical parameters of the transistors

Results & Perspectives

The semi-transparent electrodes enabled the observation of cardiomyocytes using an inverted microscope. The cells adhered well and formed a confluent network with spontaneous contraction. Additional work includes exploring the potential for monitoring cell secretion.

References

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Precision Miniaturization of 4D Printed Optical Probe Arrays

Gilgueng Hwang (Mita Lab / B. J. Kim Lab)

Keywords: Optical Microprobes, Nanoscale Aperture, Functional Miniaturization, Reconfigurable Microsystems

Context and Objectives

Reconfigurable 4D printed microstructures enable adaptive deformation and functional modulation at microscale. For precision bio-interfacing and localized optical interaction, further structural miniaturization and nanoscale aperture control are required. Develop miniaturized 4D printed optical probe arrays with tunable aperture geometry and controllable optical spot size for localized microscale actuation and sensing [1,2].

Methods

4D optical probes were fabricated using two-photon polymerization of elastomeric microstructures designed for surface-tension–driven self-closing. Controlled metallization enabled aperture miniaturization and structural reinforcement. Optical characterization was performed to evaluate tunable spot size modulation associated with reversible deformation.

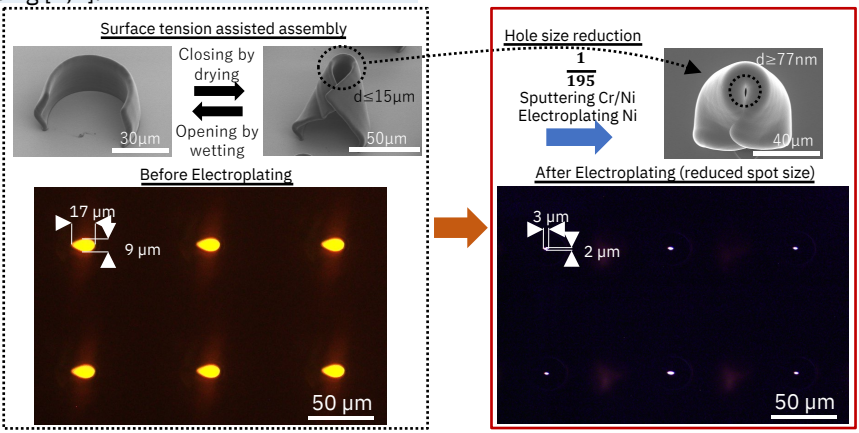

Fig. 1. Miniaturization of 4D printed optical probe arrays.

Results & Perspectives

Sub-100 nm aperture 4D optical probes were realized with tunable spot confinement. This scalable miniaturization approach enables localized bio-interaction and microscale sensing applications.

References

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Cell–Cell Interaction Studies Using a Single-Cell Pairing Microfluidic Device

Dana Simiuc & Faruk Shaik (SMMiL-E)

Keywords: Cell-cell communication, cell pairing

Context and Objectives

- Cell–cell interactions regulate multicellular communication and are crucial for the immune system's defense mechanisms. Understanding the immunological synapse (IS) is essential for developing effective immunological treatments, particularly in cancer research.
- We aim to develop a microfluidic device for high-throughput single-cell pairing of individual immune cells with leukemic cells, facilitating immune synapse formation and analysis.

Methods

- A multilayer microfluidic platform with specific geometries targeting high-throughput deterministic pairing for two different cell sizes in a unidirectional flow format.
- Introducing an auxiliary flow alters the effective channel height allowing efficient small-cell trapping.
- In short, we perform controlled high throughput single-cell pairing for immunological synapse study.

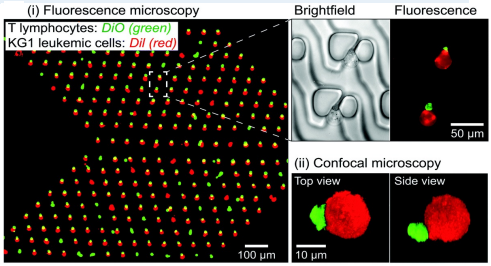

Fig.1. Cell pairing. (i) A view of paired T lymphocytes (green) and KG1 cells (red). (ii) Imaging a pair with confocal microscopy.

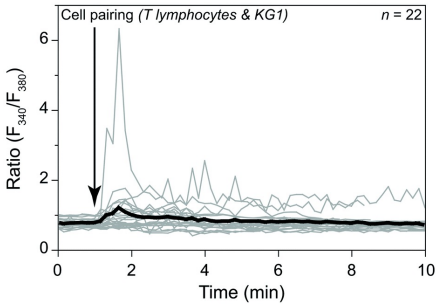

Fig.2. Cell activity monitoring. Ca^{2+} imaging experiments showing T cell activity following IS formation. Cell pairs were formed at t = 1 min.

Results & Perspectives

- T cells and leukemia cells are trap in controlled manner, at high throughput.
- IS dynamics is monitored for hours. Cell pairing is established for monitoring Ca^{2+} signature of T-cells.
- An allogenic condition was obtained by pairing primary human CD8+ T lymphocytes from healthy donors and primary AML blasts

References

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[2] Shaik F. A., et al, MicroTAS, 2022, 765-766.
[3] Shaik F. A., et al, MicroTAS, 2019, 634-635.

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Distinguishing Cancer Cells Based On Their Biophysical Properties

Jean-Claude Gerbedoen & Çagatay Tarhan (Smmil-e)

Keywords: Single-cell analysis, biophysical characterization

Context and Objectives

- Biological processes related to cells are influenced by changes in cell shape and structural integrity.
- Biophysical properties can potentially reflect the state of cells' health.
- Can we use biophysical parameters as metastatic biomarkers?
- Such biomarkers can lead to rapid and practical tools for diagnosis, disease monitoring and therapy assessment.

Methods

- Microfluidic device for cell handling
- Silicon Nano Tweezers (SNT) for biophysical measurements
- AI for distinguishing cells
  (i) SNT tips for capturing single cells.
  (ii) Actuators for manipulation & detect.
  (iii) Capacitors as displacement sensors.

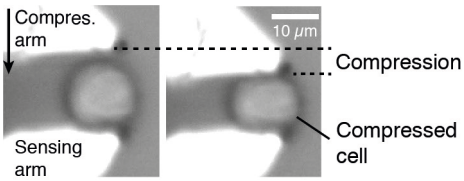

Fig.1: Compression assay with SNTs.

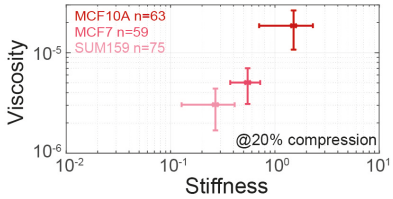

Fig.2: Comparison of cell lines with different metastatic potential. SUM159PT, the most aggressive cell lines showed the lowest stiffness and viscosity. Cell line with non-metastatic potential, i.e., MCF10A, showed the highest stiffness and viscosity.

Results & Perspectives

- SNT, integrated with microfluidics, allows single cell characterization (Fig. 1).
- Cell lines' metastatic potential followed their biophysical properties, such as viscosity and stiffness (Fig. 2).
- Obtaining biophysical signature of CTCs distinguish according to metastatic potential.
- Towards diagnostic products, drug testing platforms, disease monitoring and treatment prediction instruments.

References

[1] [1] B. Ahmadian, et al, IEEE MEMS, 317-320, 2022.
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Assessing the effects of growth factors in a lymphatic vessel-on-a-chip

Jules Edwards (Matsunaga Lab)

Keywords: Lymphatic vessel, Organ-on-chip, Growth factors, Polarization

Context and Objectives

The lymphatic vessels play a key role in tissue homeostasis and drainage of interstitial fluids. Impaired lymphatic function thus plays a role in various diseases and complications, such as secondary lymphedema or cancer. [1]

Understanding the formation of new vessels from existing ones – lymphangiogenesis – is crucial to better understand these pathologies. The use of pro-lymphangiogenic factors, such as vascular endothelial growth factor (VEGF) A and C, in a controlled environment is key to better understand this mechanism.

Methods

The lymphatic vessel-on-a-chip (LVoC), embedded in type I collagen gel, allowing us to recapitulate a controlled microenvironment. We cultivate the lymphatic vessels in VEGF-supplemented media for 3 days, during which they are monitored daily, before fixation.
By using different imaging techniques, such as basic brightfield imaging coupled with machine learning driven segmentation and immunofluorescent stainings, we are able not only to assess, but also quantify the effects of VEGFs on lymphatic vessels.

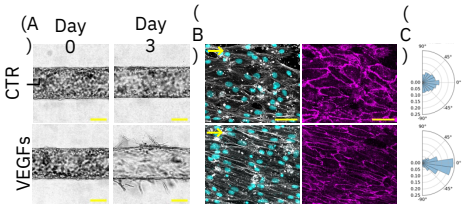

Fig.1. – Cocktail effect of VEGF A and VEGFs on the LV models. (A) Bright field microscopies. (B) Immunofluorescent stainings of F-actin and nucleus. (C) Quantification of polarity of cell nucleus. Bars: 100mm in (A) and 50mm in (B).

Results & Perspectives

Cell polarisation has been observed in lymphatic vessels as a response to shear stress [2], but polarisation by biochemical stimuli has not been reported yet. The use of inhibitors and transcriptomic analysis will allow to better understand the underlying mechanisms behind the observed synergistical effect.

References

[1] K. Alitalo, et al., Nature, 438, 946-953 (2005).
[2] K. L. Betterman et al., J Clin Invest, 130, 3315-3328 (2020).

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MIMIC : Microvessels – Impact of the Microenvironment's Intrinsic Characteristics

Baptiste Alric (Matsunaga Lab)

Keywords: Organ-on-chip, Angiogenesis, Microfabrication

Context and Objectives

Our project focuses on enhancing our knowledge of the physical characteristics of artificial microvessels and their surrounding environment[1]. Our aim is to create more precise organ-on-a-chip models by controlling this microenvironment. To achieve this, we are collaborating with partners in Japan and France to develop various cellular models and innovative methods to evaluate these physical properties[2]. Our findings underscore the critical role these properties play in microvessels physiology, structure and function[3].

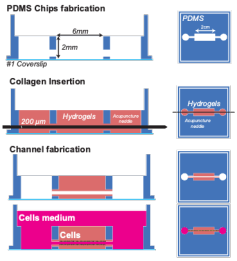

Fig.1. Microfluidics chips fabrication

Methods

We utilize custom-made microfluidic chips to construct our microvessels (see Fig. 1). We create channels by using acupuncture needles to carve pathways within hydrogels—a protein-based gel that is approximately 90% water—allowing us to culture endothelial cells in a channel-like formation.

To characterize the microenvironment, we use a novel technique that use dynamic fluid movement to assess the material's elasticity and permeability [1]. And for the microvessels we use porosity assay, bright field microscopy and confocal microscopy (see Fig. 2).

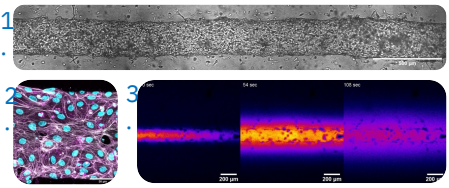

Fig.2. Microvessels Characterization (1.BF 2. Confocal microscopy 3. Porosity assay)

Results & Perspectives

These models not only deepen our insight into various biological processes but also support the development of drug screening methods to pinpoint effective treatments for specific conditions. The next step of our research is to complexify our model to be even more physiologically relevant.

References

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[2] Cacheux, Jean, et al. STAR protocols 5.2 (2024)

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Impedimetric electrochemical immunosensor for monitoring microvessel stroke models.

Pablo Rioboó-Legaspi (Matsunaga Lab)

Keywords: Electrochemistry, immunosensors, stroke.

Context and Objectives

Impedimetric immunosensors are powerful tools for monitoring proteins in a continuous and label free manner. These sensors translate the immunorecognition process into an increase in the impedance of the system when an AC is applied.

This system can be used for determination of proteins on the outlet of organ- on-a-chip models[1]. For this purpose, a microvascular stroke model comprised of human astrocytes and endothelial cells is being developed, where the release of GFAP (glial fibrillar acidic protein) can be tracked when exposed to hypoxic conditions.

Methods

An impedimetric immunosensor for GFAP was obtained by modifying a three-electrode system with a self assembled monolayer (SAM) and an anti-GFAP antibody. GFAP was chosen as it is a widely know stroke damage biomarker[2].

For the development of the stroke model, human and mouse astrocytes were evaluated, as well as different culture protocols to induce stroke-like conditions to the astrocytes in 2D and 3D.

Context and Objectives

The immunosensor presents an increase in impedance when exposed to GFAP, which can be applied to the stroke microvessel model to track the release of GFAP under hypoxia. This system can be used to deepen the understanding of the processes involved in stroke, but also for screening drugs that can promote the recovery of homeostasis.

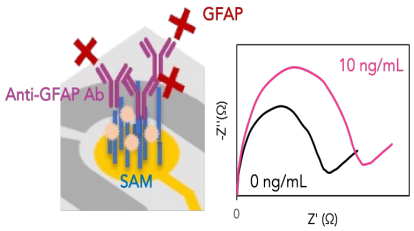

Fig.1. Sensor scheme (left) and change in EIS in the presence of GFAP (right)

Perspectives

After validating the sensor with 2D and 3D cultures, the stroke microvessel system can be coupled to a flow system and the appropriate hypoxic conditions can be applied to study the release of GFAP.

References

[1] H.M.N. Ahmad et al. Biosensors, 13, 983 (2023).
[2] C. García-Cabo et al. Cerebrovasc. Dis., 53(5), 515-518 (2023)

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Microvessel-on-a-chip for study the impact of the pressure on lymphatic vessels in the context of secondary lymphedema

Roxane Sylvestre(Matsunaga Lab)

Keywords: Lymphedema, Mechanobiology, Lymphatic vessels, Organ-on-a-chip, Microfluidics

Context and Objectives

Secondary lymphedema is a chronic condition that occurs after cancer treatments such as surgery or radiotherapy. It affects 20–40% of cancer survivors and leads to limb swelling, pain, reduced mobility, recurrent infections and major quality of life impairment.

Currently, no curative treatment exists.

A major limitation in therapy development is the poor understanding of the biological mechanisms driving the disease. In particular, the role of mechanical compression on lymphatic vessel dysfunction remains largely unknown.

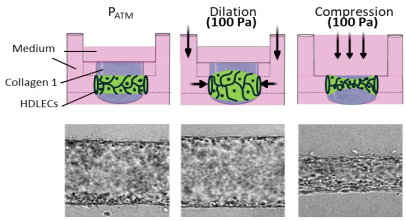
Understanding how mechanical forces alter lymphatic function could reveal new therapeutic targets

Methods

We use a microfluidic lymphatic vessel-on-chip model composed of human lymphatic endothelial cells cultured in a 3D microenvironment.

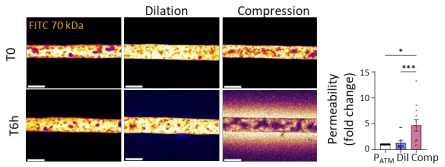
This platform allows:

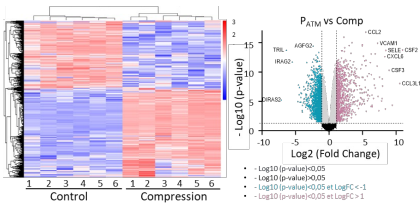
- Controlled mechanical compression
- Real-time imaging of cell behavior
- Measurement of vessel permeability
- Molecular and inflammatory analysis



Results

Mechanical compression disrupts lymphatic vessel integrity in our vessel-on-chip model. Compressed microvessels show endothelial disorganization, increased permeability and enhanced inflammatory activation compared to control conditions. These findings indicate that mechanical stress directly impairs lymphatic function and may contribute to lymphedema progression.





Perspectives

This project may reveal how mechanical forces disrupt lymphatic vessels, guiding therapies for edema in cardiovascular or inflammatory diseases.

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LiMMS Internal Project:
Microvascularized Tumor-on-a-Chip for Studying Tumor-Blood Interactions and Liquid Biopsy Applications

Baptiste Alric, Makoto Kondo, Jean Cacheux, Aurélien Bancaud, Laurent Jalabert, Yoshinobu Sugitani, Masahiro Nomura, Soo Hyeon Kim, Yukiko Matsunaga

Keywords: Artificial blood vessel, Organ-on-chip, Microfluidics

Context and Objectives

The purpose of this work is to develop a microvascularized tumor-on-a-chip platform combined with a liquid biopsy system to study tumor–blood interactions in a controlled and physiologically relevant microenvironment. The objective is to reproduce key aspects of the tumor vascular niche in vitro while enabling dynamic monitoring of tumor-derived biomarkers circulating in the bloodstream.

Although organ-on-chip technologies and liquid biopsy approaches have been developed for many years and are each well established, they are rarely integrated into a single, unified platform. Current state-of-the-art systems typically focus either on microphysiological modeling of tissues or on the detection and analysis of circulating tumor biomarkers, but seldom on their real-time interaction within the same microfluidic environment.

Methods

The novelty of this work lies in the development of a real-time microfluidic model that integrates endothelial remodeling, circulating tumor cell (CTC) capture, and exosome analysis within a vascularized tumor-on-chip device. This combined approach will allow simultaneous investigation of tumor progression, vascular dynamics, and biomarker release under physiologically relevant flow conditions.

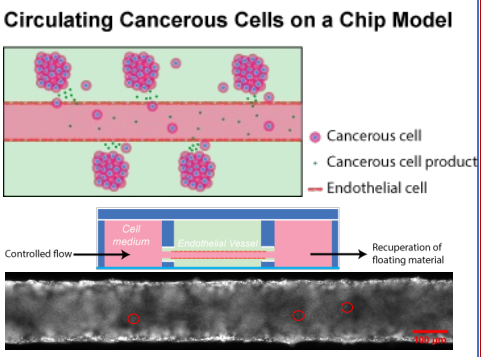

Figure 1. Nanobeads flowing at a controlled flow rate within an artificial microvessel.

Perspectives

Once completed, this project will provide a new generation of tumor-on-chip models coupled to an integrated liquid biopsy platform. Scientifically, it will generate new insights into metastatic mechanisms and tumor–vascular crosstalk. Technologically, the platform holds strong potential for intellectual property development and patent applications.

Vascular barrier models in cancer

Fabrice Soncin

Keywords: blood vessels, cancer, inflammation, immunity, microfluidics

Context and Objectives

We design blood vessels-on-chip devices to study the molecular mechanisms which regulate the vascular barrier, its immune activation, and how they participate in vessel integrity, angiogenesis, and in the extravasation of blood-borne immune cells. We also study the effects of anti-cancer therapies used in patients, such as antiangiogenics, immuno- and radiation therapies on the functions of the vascular barrier.

Methods

Blood vessels-on-chip are designed using CAD software and made in PDMS-glass devices. They are seeded with lung primary human endothelial and perivascular cells. Biological validations are performed using cell and molecular biology approaches, such as immunofluorescence and confocal microscopy, Taqman RT-qPCR and permeability and immune activation functional assays.

Context and Objectives

Alice Leroy (Univ. Lille Ph.D student, Y3) studies the effects of anti-cancer drugs on the vascular barrier and immune activation in our blood vessels on-chip models.

Ibtihal Hezili (Univ. Lille Ph.D. student, Y2) sets up a perfused blood vessel on-chip angiogenesis model to study the effects of anti-cancer drugs and radiation therapies on the vascular barrier and on angiogenesis.

Perspectives

Assess the role of biological signals & environment components on blood vessel functions, screen for active drugs and anti-cancer treatments on blood vessel permeability, activation, and angiogenesis.

References

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[2] Terrassoux L et al Small. 2025 21(45):e05343
[3] Sandoval Pacheco C et al. Mol Ther. 2025 33(12):6212-6225
[4] Sivéry A. et al. Biomicrofluidics 2025, 19, 054103

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Investigation of metabolic syndrome using organ on chip technology

Eric Leclerc (Sakai/Nishikawa Lab)

Keywords: Organ on chip, metabolic syndrome

Context and Objectives

Metabolic syndrome has a prevalence ranging to 24.6 to 34.7% of the population Japan in early 2000s and up to 36% in European countries. It implies several organ crosstalks (Fig 1). In this project we aim at developing advanced in vitro model using organ on chip technology and induced pluripotent stem cells to recapitulate the disease progression in liver, adipocytes, blood vessels and pancreas. Medooc PEPR program will be the main frame of this project, coupled with local LIMMS and ANR fundings.

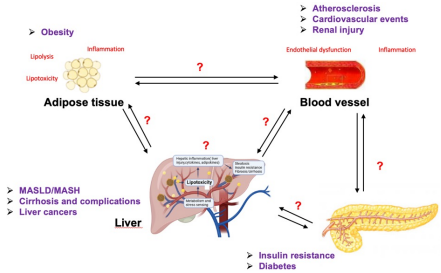

Fig.1. Mutli organ model to recapitulate organ interactions involved in the metabolic syndrome

Methods

- Organ on chip is based on silicone replica molding.
- Liver cells including hepatocytes-like cells (Fig 2A), endothelial-like cells, stellate-like cells and cholangiocyte-like cells are derived from a unique sources
- Cellular model includes adipocytes or pancreas tissues (Fig 2B) for multi organ model
- Clinical bridges to compare patient dataset and the in vitro models

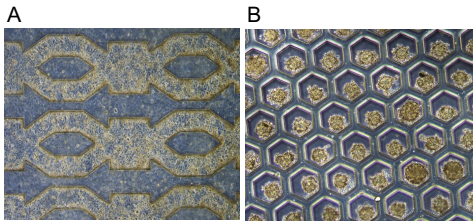

Fig.2. (A) Liver hepatocytes like cells culture in a microfluidic biochips; (B) Pancreatic spheroids made from hiPSCs beta like cells in honeycombs-based devices

Results & Perspectives

First generation of liver on chip[1], pancreas on chip[2], adipocytes on chip were proposed. Liver adipocytes and liver pancreas crosstalk were also investigated. Disease configurations are now under investigations.

References

[1] Wang et al., J of Applied Tox 2025
[2] Morisseau et al., M Omics, 2023

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iPS-cells derived 4-culture Liver organ-on-chip model for metabolic syndrome

Dhimas Agung Kurniawan (Sakai-Nishikawa Lab)

Keywords: liver, organ-on-chip, iPS-cells, NAFLD

Context and Objectives

Non-alcoholic fatty liver disease (NAFLD) has become one of the leading chronic liver diseases worldwide, yet human-relevant experimental models remain limited. Animal models often fail to fully recapitulate human metabolic and inflammatory responses, while traditional two-dimensional cell cultures lack multicellular interactions critical for disease progression. In particular, the interplay between hepatocytes, resident macrophages (Kupffer cells), endothelial cells (LSEC), and stellate cells (HSC) determines the transition of the disease.

The objective of this project is to develop a human iPS cell-derived four-cells liver organ-on-chip model with dynamic microfluidic environment to reproduce key cellular interactions driving NAFLD.

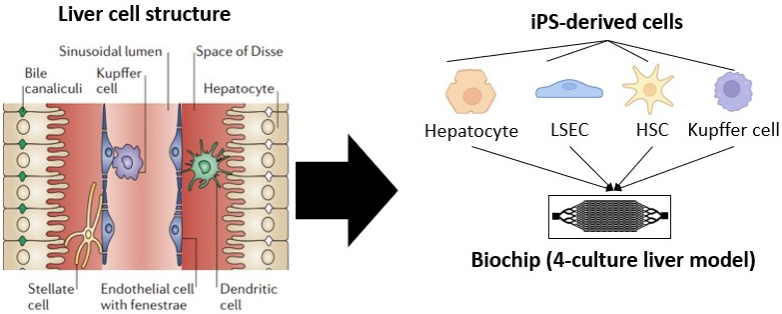

Fig.1. Structure of cells in the liver (left) are modeled by this 4-culture model in the biochip (right). Key cell interactions critical to the NAFLD progression to be studied through omics analysis.

Methods

iPS-derived hepatocyte-like cells, LSEC and HSC are prepared according to previously developed study [1]. In addition with Kupffer cells, are seeded into the organ-on-chip until sufficiently stable and mature.

Followingly, inducement of NAFLD is initiated by addition of fatty acid into the culture. Multicellular interactions are then studied through metabolomics and transcriptomics analysis

References

[1] Scheidecker, B. et al. Biofabrication 16.2 (2024): 025037

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Investigation of Non-alcoholic Fatty Liver Disease by Organ-on-a-chip.

Wang Hanyuan (Sakai & Nishikawa Lab)

Keywords: Liver Organ-on-a-chip, HepaSH, palmitic acid, steatosis

Context and Objectives

Non-alcoholic Fatty Liver Disease (NAFLD), a complex disorder with a high worldwide prevalence, is one of main cause of critical liver diseases. The lack of therapeutic solution of NAFLD leads to an unmet need to develop an efficient in vitro disease model to investigate its onset, propagation and the effects of drugs.

In our study, we used organ-on-a-chip technology to test palmitic acid (PA) on a HepaSH liver model to reproduce and investigate the disease progression[1].

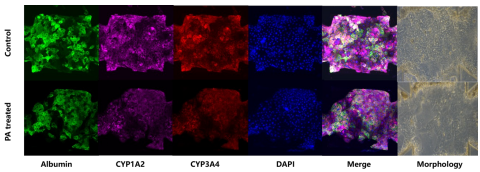

Fig.2. Microscopic morphologies after PA exposure; Immunostaining of Albumin, CYP1A2, CYP3A4 in control and PA treated biochips.

Results & Perspectives

The exposure of the HepaSH to PA shew an increased ROS and IL-6 secretions, altered gene expression on lipid metabolism, the p38/MAPK/NFKB route, and the mitochondrial processes. Additional time points analysis and more comprehensive fatty acids exposusure ought to be proceeded.

Methods

HepaSH cells were provided by Kacnet (Japan), freshly seeded in collagen-coated biochips right after one day shipment. After 2 days of static culture and 4 days of perfusion culture, the cells were exposed to 0.5 mM PA for 14 days.

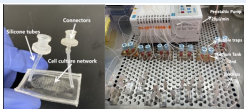

Fig.1. Biochips and perfusion setup

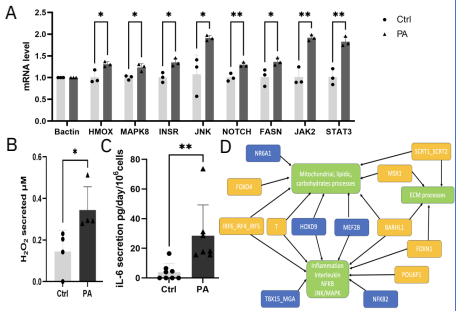

Fig.3. Compatison in control and PA treated cells of the mRNA expression (A), ROS secretion (B) and IL-6 secretion (C); tentative regulatory network bridging the top activated transcription regulators (blue for control; orange for PA treated cells) (D).

References

[1] H.Wang et al. Toxicology, Feb. 2026, Volume 520

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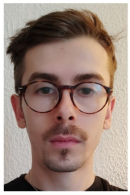
New adipocyte/Liver-on-chip model for studying metabolic diseases

Augustin Brassens, Cécile Legallais, Eric Leclerc, Rachid Jellali

Keywords: Organ-on-chip, Adipocyte, Hepatocyte, Microfluidic, MASLD



Context and Objectives

Adipose tissue is essential for energy storage, endocrine signaling, and inflammation regulation [(1)]. 2D cultures and animal models lack physiological relevance and translatability to humans. Organ-on-chip technology enables the recreation of human-like microenvironments in vitro [(2)].

Objectives are to develop an adipocyte-on-chip model to provide a reliable tool for investigating crosstalk metabolic mechanisms and drug responses in a human-relevant context.

Methods

- Microfluidic chip: 3D culture
- Cell line: immortalized human
- mesenchymal stem cells (hMSCs)
- Validation through: Lipid accumulation (Oil Red, LIPIDTOX staining) Gene expression (PPARγ, FABP4)
- Coupling with hepatocyte on-chip

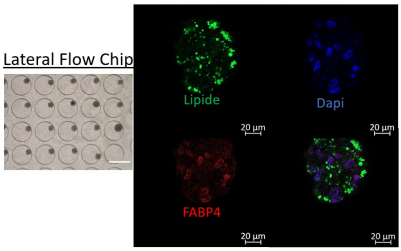


Fig.1. Figure showing adipocyte spheroids directly generated within the microfluidic chip. Immunofluorescence staining of lipid vacuoles and FABP4. Scale bar: 400 µm.

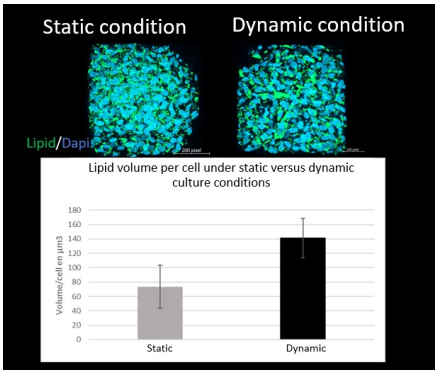


Fig.2. Comparison of lipid content per cell in static versus dynamic spheroids. Quantification was performed using confocal Z-stack analysis.

Results & Perspectives

Lipid storage and endocrine function were maintained in both conditions.

Dynamic culture promoted the formation of larger lipid vacuoles compared to static spheroids.

Future work will focus on establishing an adipocyte–hepatocyte co-culture system.

References

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[2] Brooks, E. et al. (2017). Cell Reports, 21(2), 311–323.

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LiMMS Internal Project
Integration of in vitro/in vivo omics data in to a in silico steatosis model

Eric Leclerc[1], Hanyuan Wang[1], Fabrice Soncin[2], Yasuyuki Sakai[1]

[1]Sakai lab, [2]SMMiLE

Keywords: Liver in vitro and in silico modelling, clinical data, steatosis

Context and Objectives

In order to build relevant in silico model of liver steatosis[1], there is a need of dataset to calibrate and validate model parameters

The technologies of organ on chip and liver organoids can reproduce partially the physiology of the hepatic tissue allowing to collect biofluid sample useful for biomarker extraction[2].

The clinical cohorts publicly available and real dataset can permit the extraction of clinical features of patients and the comparison with in vitro data.

Methods

- Organ on chip experiments
- Steatosis model using free fatty acids
- Metabolomics profile of in vitro data
- Collect of metabolomics and clinical features from literatures
- Statistics analysis
- Discussion with clinicians

Results

Metabolites signatures were measured from

- Organ on chip of healthy liver culture
- Organ on chip data exposed to free fatty acids

Collection of data from patient cohorts

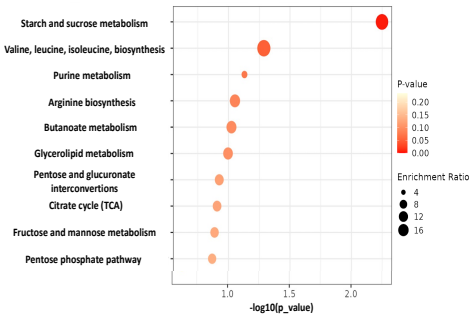

Fig.1. Enrich pathway by the metabolites detected by metabolomics differentially expressed between control organ on chips and organs on chip exposed to free fatty acid.

Perspectives

Comparison of in vitro/in vivo data,

Integration of new patients' cohort data,

Mathematical model calibration

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[1] Miura et al., Tox Sciences, 2026

[2] Wang et al., J of Applied Tox 2025

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Development of a liver digital twin for liver disorders analysis

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Keywords: Liver Digital Twin, Simulation

Context and Objectives

Liver diseases from none alcoholic fatty liver disease to liver hepatocarcinoma, drug induced liver injury, remain a high leading causes of morbidity. Traditional preclinical rely on in vitro assays, animal models and in silico modeling. Among them digital twin are multiscale models trying to integrate organism to cellular biological patterns offering counterfactual exploration (diet[1,2], dosing, gene perturbations, metabolism[1,2], drugs[1]). In this frame we proposed a liver model to investigate lipid metabolism and steatosis onset.

Methods

- Agent based model
- Multi cellular features including fluid flow dynamics, molecular diffusion and active transports, metabolism
- GPU/Cuda environment for parallel computing
- Graphical interface for friendly user utilization
- Simulations of case studies such as postprandial lipid input, Fatty diet chronic exposures, inflammation, etc...

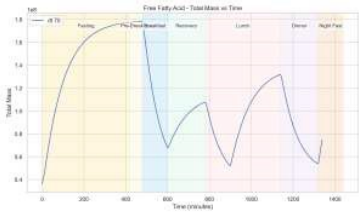

Fig.1. Example of free fatty acid time course simulations in response to various types of fasting/feeding transitions

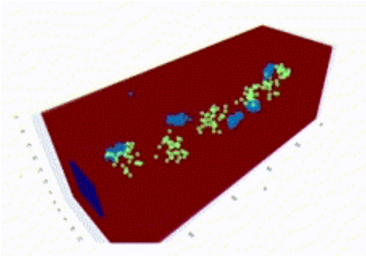

Fig.2. Example of growing stellate and macrophage cells inside a 3D sinusoid liver structure in response to stress

Results & Perspectives

A liver sinusoidal like structure was build six cellular agents. 15 species can be used to describe the liver metabolisms. Rules were implemented to recapitulate the onset of liver disorders such as steatosis and heatly/pathological typical clinical dynamics (Figs 1 and 2).

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LiMMS Internal Project

Liver Function and Disease Dynamics by Agent-Based Numerical Models

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Keywords: Agent-based modelling, Microfluidics, Organoids

Context and Objectives

Interfacing in vitro model such as liver microfluidics + in silico artificial organoids, with computer models by agent-based methods (ABM).

The multicellular microfluidic platform reproduces the physiology of the hepatic sinusoid, generating data input to build a complex model of artificial liver tissue.

The 2D-3D model will reproduce the different cell populations, the experimental environment and functional gradients along microfluidic flows.

Results

A user-friendly computer model demonstrator that will include:

- Proof of concept
- Application to real images from the micro platform and clinical histology

Perspectives

The technological workflow designed with the integration of in vivo and in vitro knowledge for ABM simulation will be translated to the disease simulation of pathologies.

Methods

- Integrated Fortran90-Python workflow
- Graphical user interface for data input and postprocessing
- Agent based model

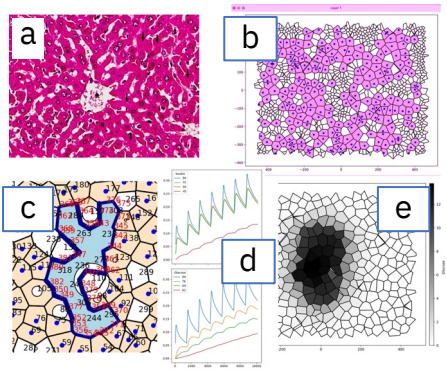

Fig.1. (a) Histological section of liver lobule. (b) Simulated reconstruction of the image. (c) Evolution of fibrotic tissue (blue) around a sinusoid (light blue), fat accumulation (white) among hepatocytes (pink). (d) Time plots of insulin and glucose. (e) Oxygen diffusion map around the sinusoid.

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